**ASX Release**

16 October 2024

## INVESTOR PRESENTATION

**MELBOURNE, AUSTRALIA 16 October 2024:** Arovella Therapeutics Ltd (ASX: ALA), a biotechnology company focused on developing its invariant Natural Killer T (iNKT) cell therapy platform, is pleased to provide an update to investors in the form of the attached presentation.

The presentation will be used in Arovella's non-deal investor meetings being conducted this week.

The presentation is attached to this announcement and can be viewed on the Company's website www.arovella.com.au.

*Release authorised by the Managing Director and Chief Executive Officer of Arovella Therapeutics Limited.*

**Dr Michael Baker**
**Chief Executive Officer & Managing Director**
**Arovella Therapeutics Ltd**
Tel +61 (0) 403 468 187
investor@arovella.com

**NOTES TO EDITORS:**

**About Arovella Therapeutics Ltd**

Arovella Therapeutics Ltd (ASX: ALA) is a biotechnology company focused on developing its invariant natural killer T (iNKT) cell therapy platform from Imperial College London to treat blood cancers and solid tumours. Arovella's lead product is ALA-101. ALA-101 consists of CAR19-iNKT cells that have been modified to produce a Chimeric Antigen Receptor (CAR) that targets CD19. CD19 is an antigen found on the surface of numerous cancer types. iNKT cells also contain an invariant T cell receptor (iTCR) that targets glycolipid bound CD1d, another antigen found on the surface of several cancer types. ALA-101 is being developed as an allogeneic cell therapy, which means it can be given from a healthy donor to a patient. Arovella is also expanding into solid tumour treatment through its CLDN18.2-targeting technology licensed from Sparx Group. Arovella will also incorporate its IL-12-TM technology into its solid tumour programs.

**Glossary: iNKT cell** – invariant Natural Killer T cells; **CAR** – Chimeric Antigen Receptor that can be introduced into immune cells to target cancer cells; **TCR** – T cell receptors are a group of proteins found on immune cells that recognise fragments of antigens as peptides bound to MHC complexes; **B-cell lymphoma** – A type of cancer that forms in B cells (a type of immune system cell); **CD1d** – Cluster of differentiation 1, which is expressed on some immune cells and cancer cells; **aGalCer** – alpha-galactosylceramide is a specific ligand for human and mouse natural killer T cells. It is a synthetic glycolipid.

For more information, visit www.arovella.com

This announcement contains certain statements which may constitute forward-looking statements or information ("forward-looking statements"), including statements regarding negotiations with third parties and regulatory approvals. These forward-looking statements are based on certain key expectations and assumptions, including assumptions regarding the actions of third parties and financial terms. These factors and assumptions are based upon currently available information, and the forward-looking statements herein speak only of the date hereof. Although the expectations and assumptions reflected in the forward-looking statements are reasonable in the view of the Company's directors and management, reliance should not be placed on such statements as there is no assurance that they will prove correct. This is because forward-looking statements are subject to known and unknown risks, uncertainties and other factors that could influence actual results or events and cause actual results or events to differ materially from those stated, anticipated or implied in the forward-looking statements. These risks include but are not limited to: uncertainties and other factors that are beyond the control of the Company; global economic conditions; the risk associated with foreign currencies; and risk associated with securities market volatility. The Company assumes no obligation to update any forward-looking statements or to update the reasons why actual results could differ from those reflected in the forward-looking statements, except as required by Australian securities laws and ASX Listing Rules.

ASX:**ALA**

arovella
THERAPEUTICS

# Investor Lunch

## October

2024

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# Arovella's strengths

### Off-the-Shelf iNKT Cell Platform

Developing off-the-shelf iNKT cell therapies to target blood cancers and solid tumour cancers

### Lead Product Advancing to Clinic

ALA-101, potential treatment for CD19-positive blood cancers, progressing to Phase 1 clinical trials, expected to commence in FY2025

### Addressing Key Unmet Need

Our iNKT cell platform is well positioned to solve key challenges that hamper the cell therapy sector

### Strong Leadership Group

Leadership team and Board have proven experience in drug development, particularly cell therapies

### Strategic Acquisitions

Focused on acquiring innovative technologies that strengthen its cell therapy platform and align with its focus areas

### Unique Value Proposition

Arovella is among few companies globally developing an iNKT cell therapy platform

# Financial overview

## Financial Snapshot

| ASX CODE | ALA |
|---|---|
| Market capitalisation[1] | $194.59 million |
| Shares on issue | 1,051.8 million |
| 52-week low / high[1] | $0.074 / $0.190 |
| Cash Balance (30 June 30, 2024) | $12.7 million |

## Major Shareholders

| Shareholder | Ownership (%) [1] |
|---|---|
| BIOTECH CAPITAL MANAGEMENT PTY LTD | 109,709,355 (10.49%) |
| RICHARD JOHN MANN | 64,458,288 (6.14%) |
| UBS NOMINEES PTY LTD | 25,620,196 (2.45%) |
| BLACKBURNE CAPITAL PTY LTD | 21,227,306 (2.03%) |
| MR JAMES EVAN HUGHES-MORRIS | 19,688,196 (1.87%) |

1. *As of 14 October 2024*

# Recent cell therapy transactions[1]

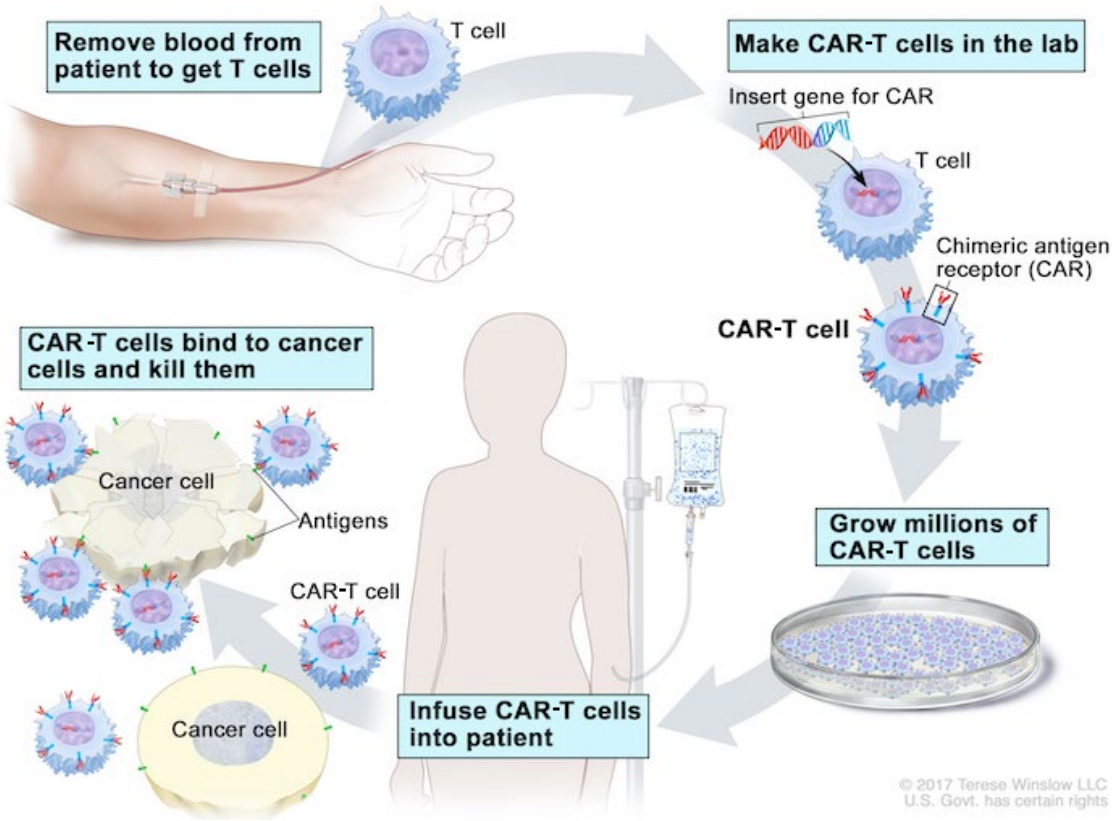
| Date | Type of deal | Acquirer/Licensee | Target/Licensor | Cell Type | Stage | Upfront (US$M) | Milestones (US$M) | Total deal value (US$M) |
|---|---|---|---|---|---|---|---|---|
| May-24 | Research collaboration | Xyphos | Poseida Therapeutics | T cell | TBD | $50 | $550 | $600 |
| Dec-23 | Acquisition | AstraZeneca | Gracell | T Cell | Phase 1b | $1,000 | $200 | $1,200 |
| Nov-23 | Collaboration and investment[2] | AstraZeneca | cellectis | Not specified | Platform | $25 | $70-220 per product | |
| Aug-23 | Licence[3] | IMUGENE Developing Cancer Immunotherapies | Precision Biosciences | T Cell | Phase 1b | $21 | $206 | $227 |
| Aug-23 | Strategic investment (ROFR) [4] | astellas | Poseida Therapeutics | T Cell | Phase 1 | $25 | $0 | $25 |
| May-23 | Licence | janssen | CBMG Cellular Biomedicine Group | T Cell | Phase 1b | $245 | *undisclosed* | |
| Jan-23 | Acquisition | AstraZeneca | neogene Therapeutics | T Cell | Phase 1 | $200 | $120 | $320 |
| Oct-22 | Development collaboration[5] | Gilead | Arcellx | T Cell | Phase 2 | $225 | *undisclosed* | |
| Sep-22 | Research collaboration | Genentech A Member of the Roche Group | ArsenalBio | T Cell | Preclinical | $70 | *undisclosed* | |
| Aug-22 | Licence & strategic collaboration | Roche | Poseida Therapeutics | T Cell | Phase 1 | $110 | $110 | $220 |
| Sep-21 | Development collaboration | Genentech A Member of the Roche Group | Adaptimmune | T Cell | Preclinical | $150 | $150 | $300 |
| Aug-21 | Research collaboration | Gilead | APPIA BIO | iNKT Cell | Preclinical | *undisclosed* | *undisclosed* | $875 |
| May-21 | Acquisition | Athenex | kuur Therapeutics | iNKT Cell | Phase 1 | $70 | $115 | $185 |
| Jun-21 | Acquisition | eterna | Novellus Therapeutics | Multiple | Preclinical | $125 | $0 | $125 |

*1. See the last slide for deal references; 2. Cellectis will receive a US$220m equity investment from Astra Zeneca plus tiered royalties. Milestones are payable for 10 products; 3. Precision is eligible for double digit royalties on net sales and $145 million in milestone payments and tiered royalties for additional programs; 4. Poseida also received a US$25m equity investment from Astellas; 5. Arcellx also received a US$100m equity investment from Gilead*

# About CAR-T cells

# How original CAR-T cell therapies work

## CAR-T cell therapy is personalised medicine




### T cells = immune cell

T cells are a common type of immune cell that fight infections and can help fight cancer.

### T cells from patient 'reprogrammed'

To generate autologous CAR-T cells, T cells are taken from a patient with blood cancer and 'reprogrammed' to produce a Chimeric Antigen Receptor (CAR). The CAR can recognise cancer cells through a target antigen.

### CAR-T cells find & kill tumour cells

CAR-T cells are administered to the patient to find and kill the tumour cells. Once the CAR binds to a tumour cell, the CAR-T cell is activated to kill the tumour cell.

https://www.ohsu.edu/sites/default/files/2021-04/CAR%20TcellTherapy7-700px.jpg

# Cell Therapy has revolutionised blood cancer treatment

## CAR-T cells have demonstrated their curative potential in blood cancers

The Cell Therapy market is expected to reach

**$61.2 billion**

by 2030[1]

### Cure

CAR-T cells have demonstrated ability to **cure haematological cancers**

### Strong Sales

### 40-60%

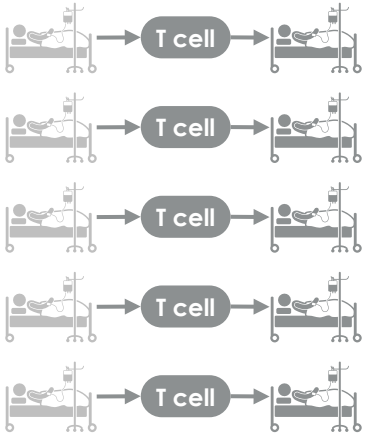
Patients relapse post-CAR-T therapy[2]

| Product | Approval Year | 2023 Revenue |
|---|---|---|
| YESCARTA® (axicabtagene ciloleucel) | 2017 | US$1498m[3] |
| KYMRIAH® (tisagenlecleucel) | 2017 | US$509m[4] |
| Abecma® (idecabtagene vicleucel) | 2021 | US$472m[5] |


1. *https://www.businesswire.com/news/home/20230529005130/en/Global-Cell-Therapy-Market-Report-2023-Advancements-in-Biotechnology-Drives-Growth---ResearchAndMarkets.com*
2. *Zinzi et al., 2023 Pharmacological Research - 10.1016/j.phrs.2023.106742*
3. *https://www.gilead.com/news-and-press/press-room/press-releases/2024/2/gilead-sciences-announces-fourth-quarter-and-full-year-2023-financial-results#:~:text=Yescarta%C2%AE%20(axicabtagene%20ciloleucel)%20sales,%E2%80%9D)%20outside%20the%20United%20States.*
4. *https://www.novartis.com/sites/novartis_com/files/2024-01-interim-financial-report-en.pdf*
5. *https://news.bms.com/news/details/2024/Bristol-Myers-Squibb-Reports-Fourth-Quarter-and-Full-Year-Financial-Results-for-2023/default.aspx*

# Current CAR-T technology challenges

One CAR-T product **only** treats the patient who supplied the T cells



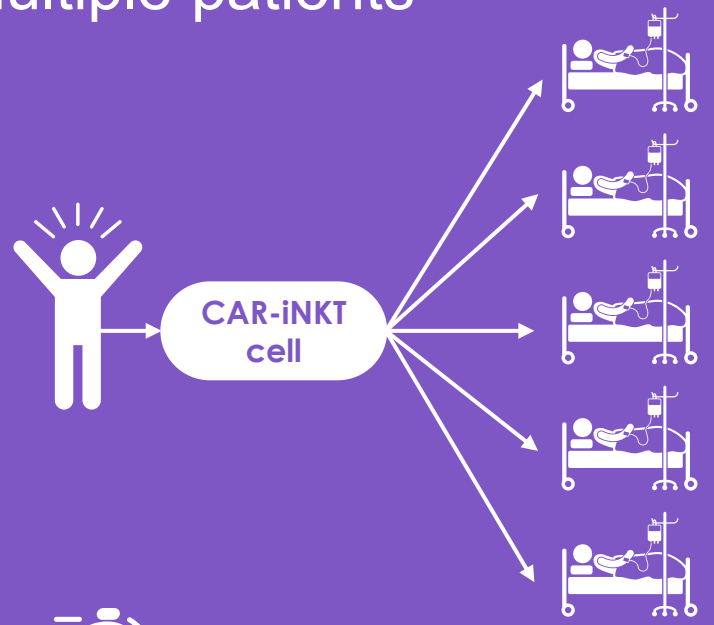

Each manufacturing batch is **patient-specific**

Patient must wait **3-4 weeks** for therapy

- Manufacturing & supply chain **costs are high**
- T cells **can be compromised** due to disease
- **Limited centres** can collect and manufacture
- **Time is an issue** for patients with aggressive disease
- Manufacturing run **failures can occur**

# ALA's solution:

One CAR-iNKT batch from **a healthy donor** treats multiple patients

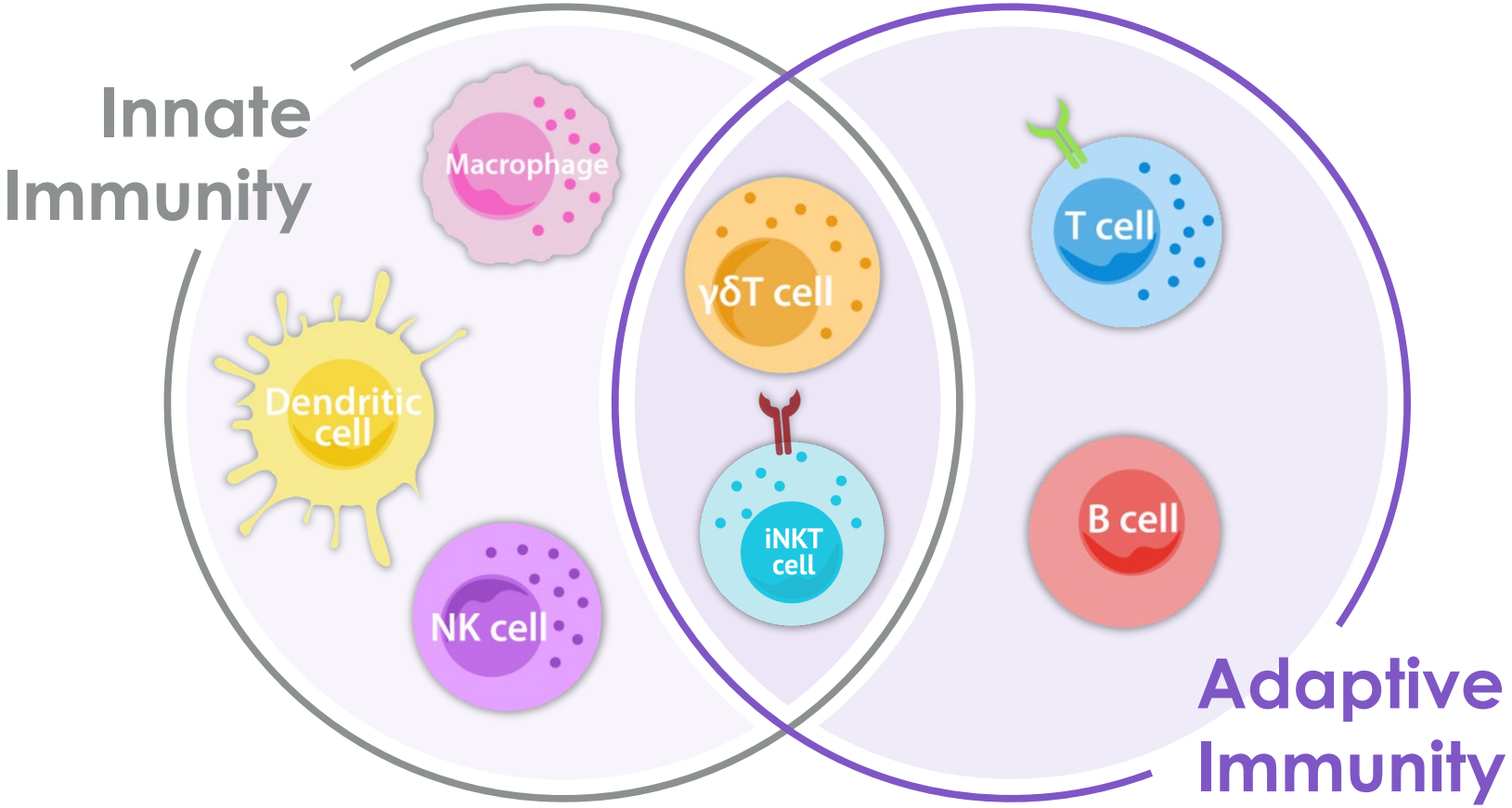



## 1 week

Patients ready to dose within 1 week

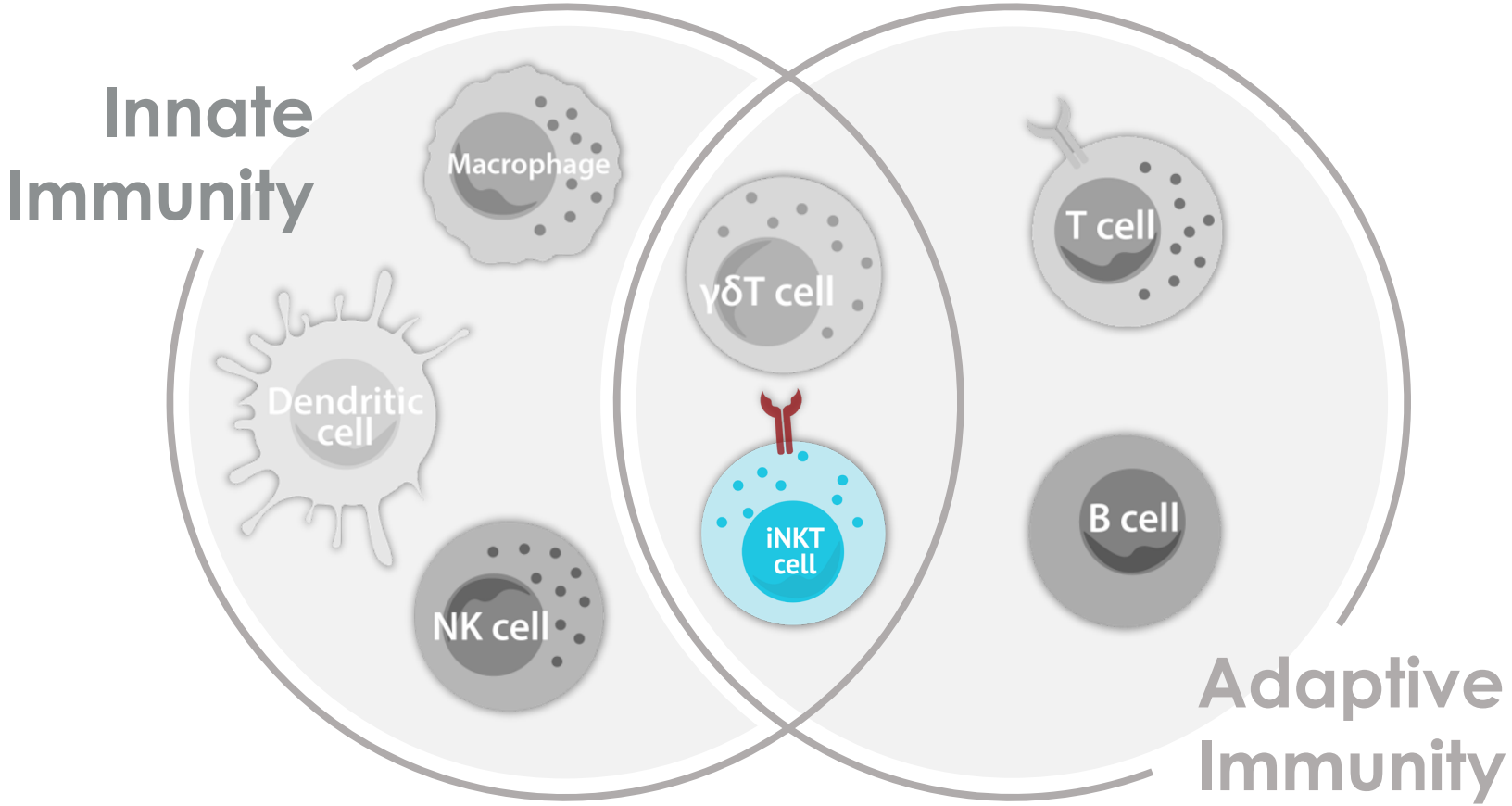
# Introducing invariant Natural Killer T (iNKT) cells

## Bridging the innate and adaptive immune system



# iNKT cells represent a next-generation cell therapy

## Properties make them ideal for use in cell therapy




### Strong safety profile

- Don't cause graft versus host disease (GvHD)

### Front line of the human immune system

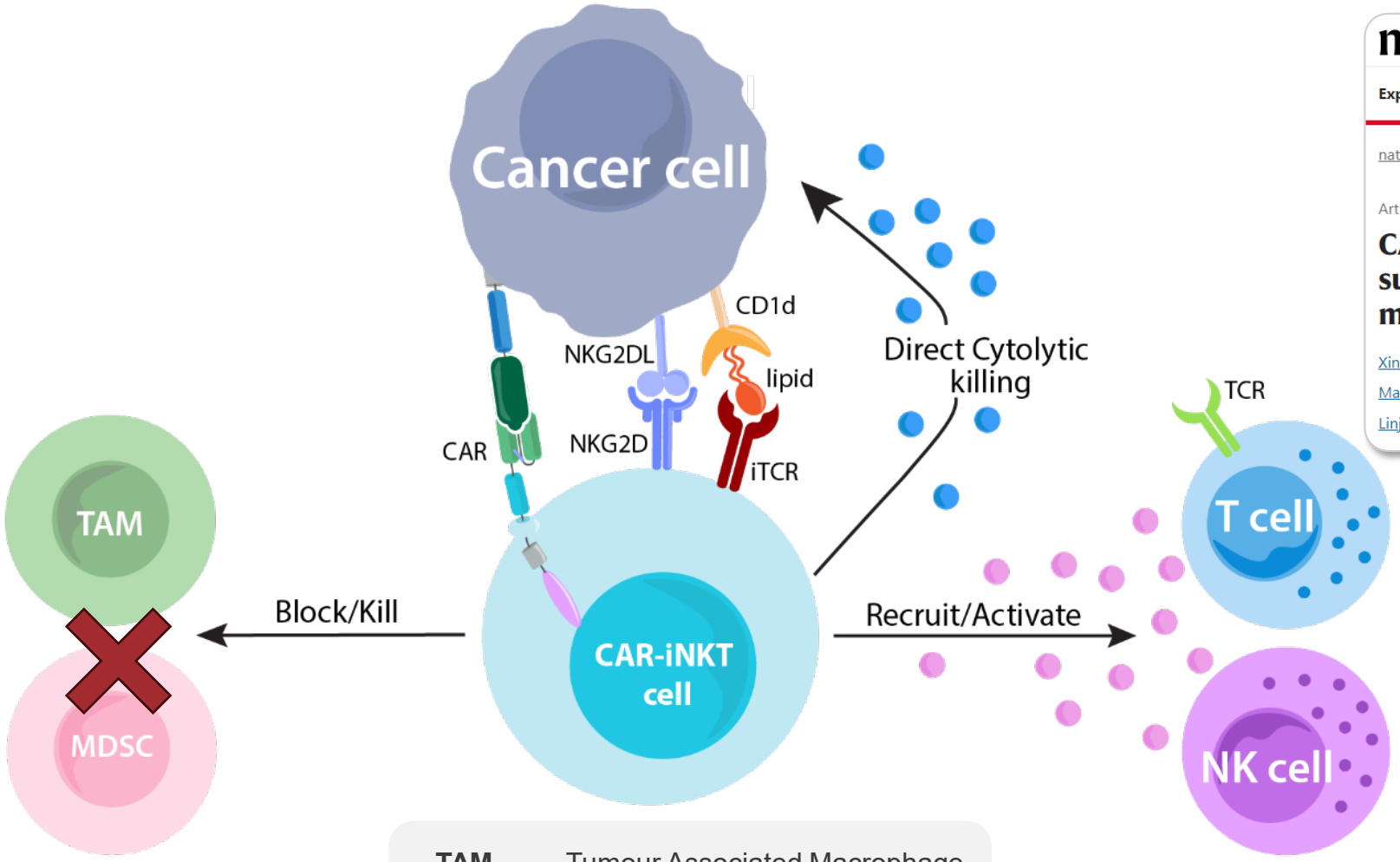
- Bridge innate & adaptive immune responses
- Contain both T cell & NK cell killing mechanisms
- Naturally target & kill cancers that express CD1d

### Multiple anti-cancer properties

- Shape the tumour microenvironment by blocking/killing pro tumour cells (TAMs/MDSCs)
- Infiltrate tumours & secrete signaling molecules to activate other immune cells to kill tumour cells

# CAR-iNKT cells have multiple ways to kill cancer cells

## Also recruit 'good' immune cells and block 'bad' immune cells




| | |
|---|---|
| **TAM** | Tumour Associated Macrophage |
| **MDSC** | Myeloid Derived Suppressor Cell |
| **CAR** | Chimeric Antigen Receptor |
| **NK** | Natural Killer |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Article | Published: 01 October 2024

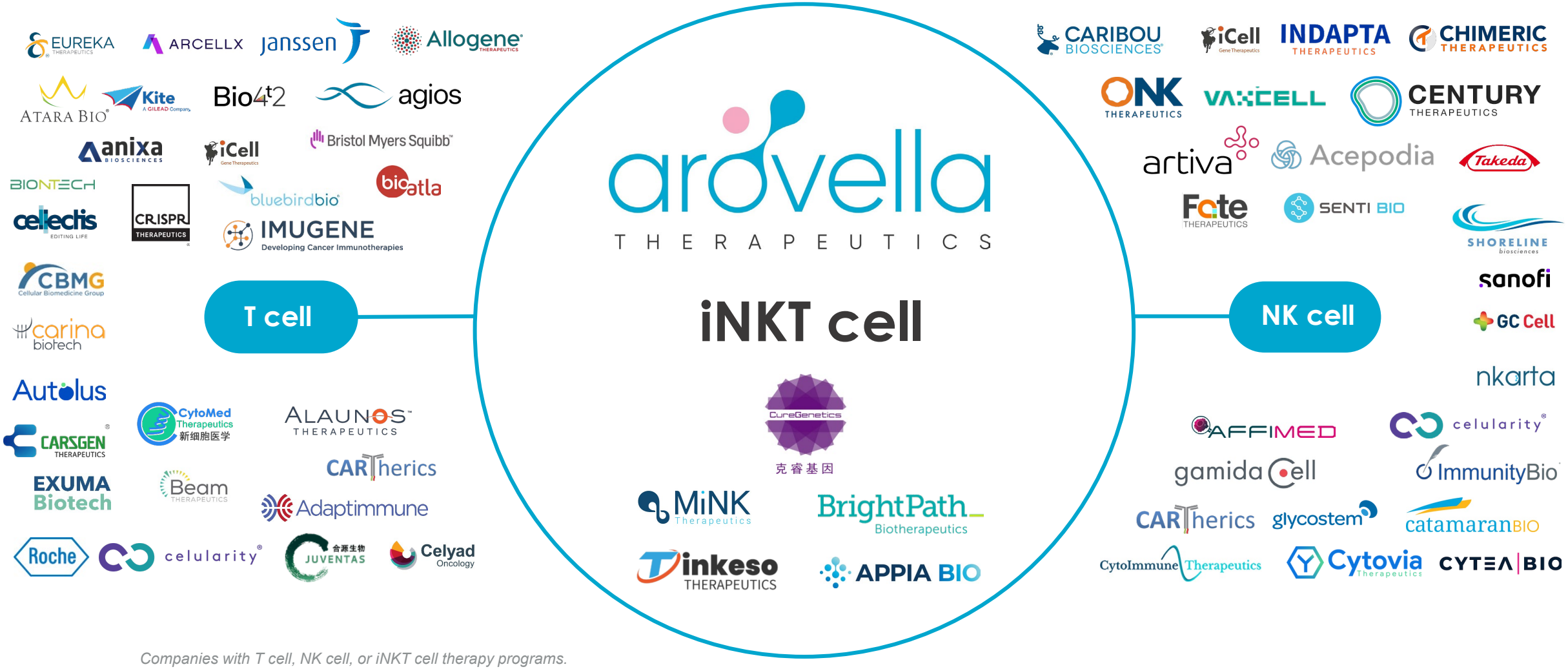

**CAR-redirected natural killer T cells demonstrate superior antitumor activity to CAR-T cells through multimodal CD1d-dependent mechanisms**


Xin Zhou, Ying Wang, Zhangqi Dou, Gloria Delfanti, Ourania Tsahouridis, Caroline Marnata Pellegry, Manuela Zingarelli, Gatphan Atassi, Mark G. Woodcock, Giulia Casorati, Paolo Dellabona, William Y. Kim, Linjie Guo, Barbara Savoldo, Ageliki Tsagaratou, J. Justin Milner, Leonid S. Metelitsa & Gianpietro Dotti


1. **Via the CAR**
   - Specific target depending on tumour type
2. **Via the NKG2D pathway**
   - NKG2D ligands are upregulated in cancer cells
3. **Via lipid-bound CD1d**
   - Several cancers naturally express CD1d

# A differentiated position

## T cell and NK cell sectors are competitive




*Companies with T cell, NK cell, or iNKT cell therapy programs.*
*Source: Company analysis based on public information*

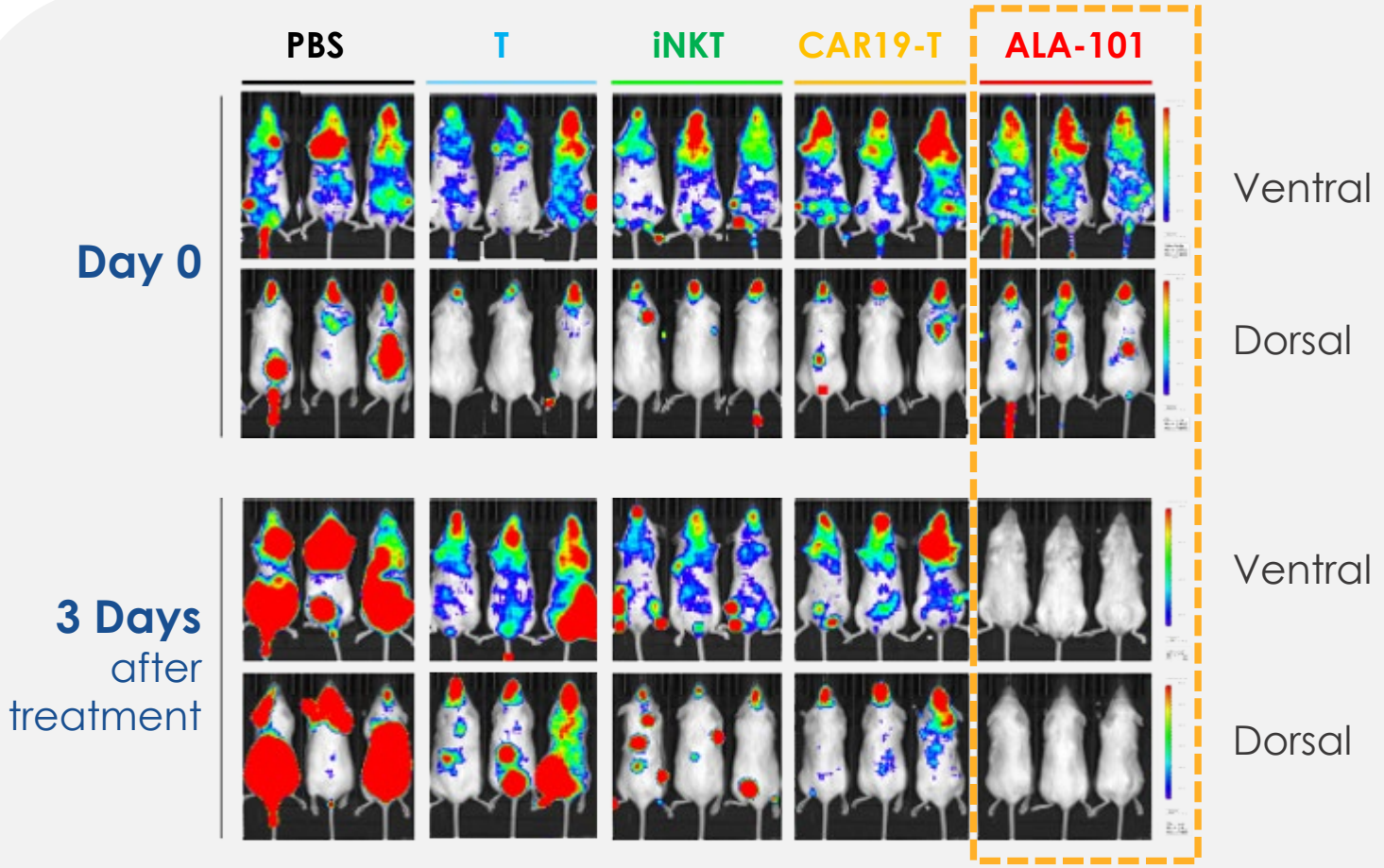
# ALA-101 (CAR19-iNKT cells)

A next generation **off-the-shelf** cell therapy for CD19-positive cancers

# ALA-101: enhanced tumour killing *in vivo*

## ALA-101 rapidly eradicates tumour cells in mice

- Tumour cells positive for **CD19** and **CD1d** were intravenously delivered into mice
- Mice were treated with:
  - PBS (saline)
  - Unmodified T cells (T)
  - Unmodified iNKT cells (iNKT)
  - CAR19-T cells
  - ALA-101 (CAR19-iNKT cells)
- After three days, ALA-101 resulted in significant regression of tumour cells
- In all other treatments, there was strong tumour cell persistence
- ALA-101 displays swift action

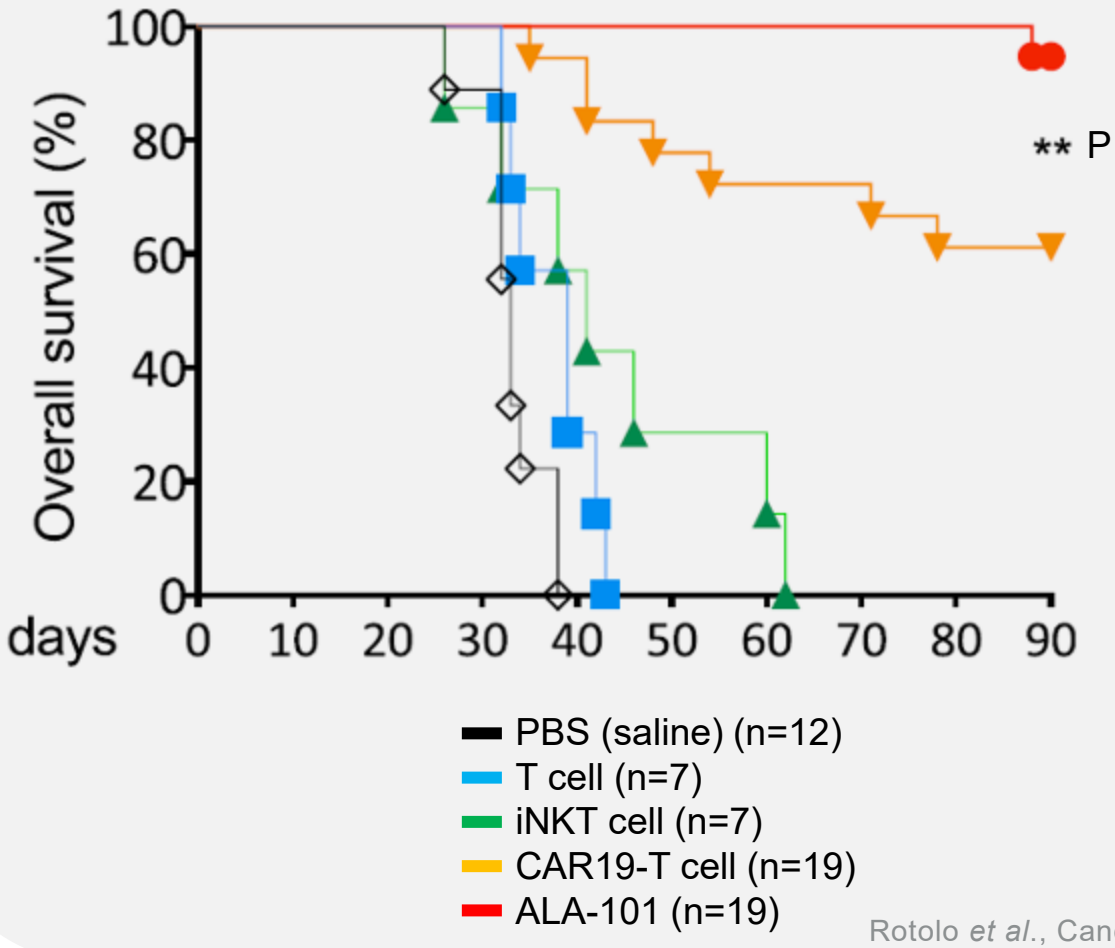



Rotolo *et al.*, Cancer Cell (2018)

# ALA-101: next generation cell therapy

## ALA-101 significantly increased survival in mice versus treatment with CAR19-T cells

- Tumour cells positive for **CD19** and **CD1d** were intravenously delivered into mice
- Mice were treated with:
  - PBS (saline)
  - Unmodified T cells (T)
  - Unmodified iNKT cells (iNKT)
  - CAR19-T cells
  - ALA-101 (CAR19-iNKT cells)
- After 90 days, only mice treated with CAR19-T cells or ALA-101 remained alive
- 1.5x more mice treated with ALA-101 remained alive after 90 days relative to CAR19-T cells
- ALA-101 has the potential to be an effective, off-the-shelf cell therapy for the treatment of CD19-positive cancers

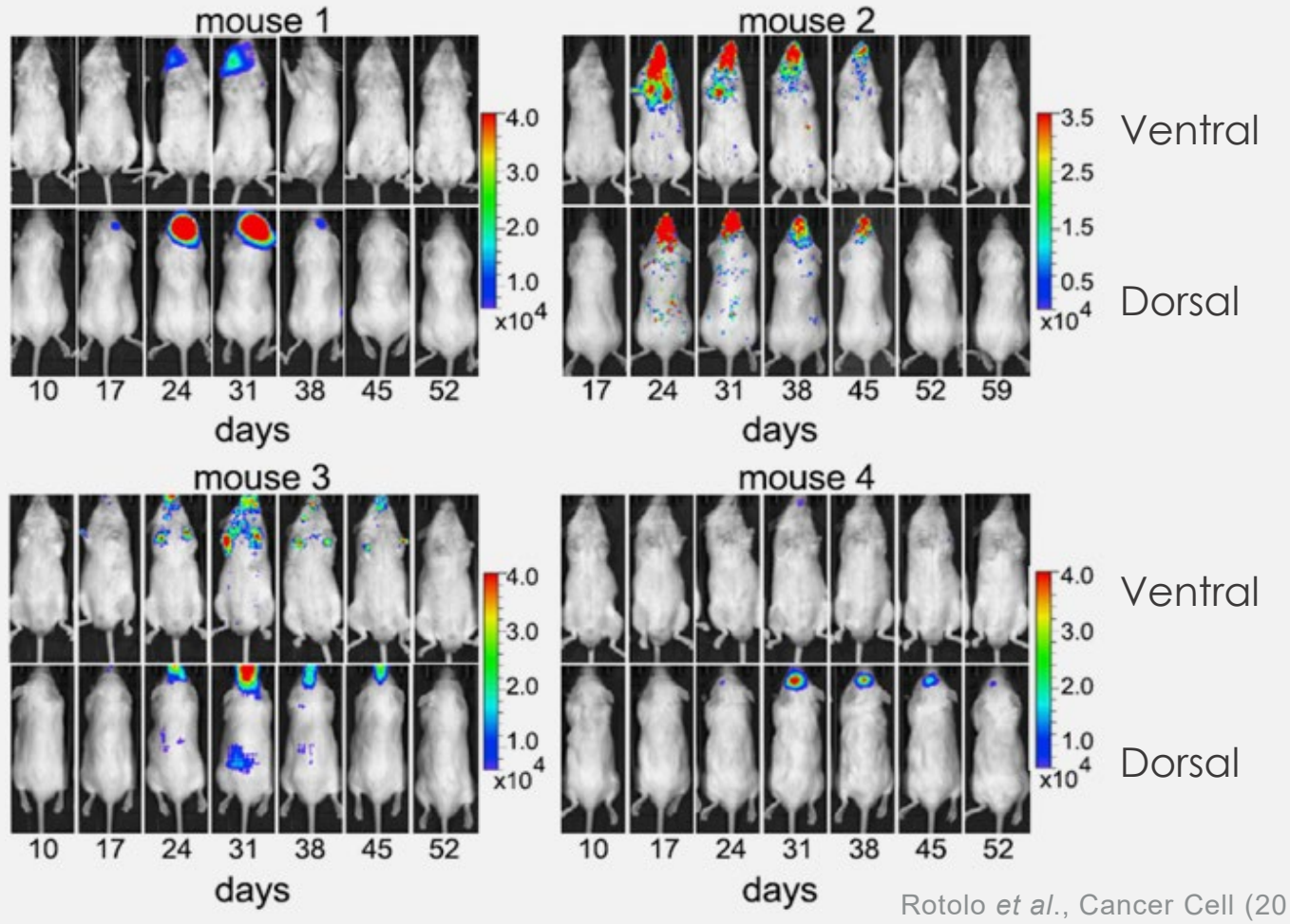



Rotolo *et al.*, Cancer Cell (2018)

# ALA-101: spontaneous secondary remission

## ALA-101 activity may persist to eradicate tumour cells following relapse

- Four mice treated with ALA-101 had the cancer return to the brain
- In all four mice, the cancer was eliminated a second time with no additional dosing
- This provides evidence that CAR19-iNKT cells can survive and continue to protect against cancer cells in vivo
- Potential to use ALA-101 to treat central nervous system lymphoma or brain metastases

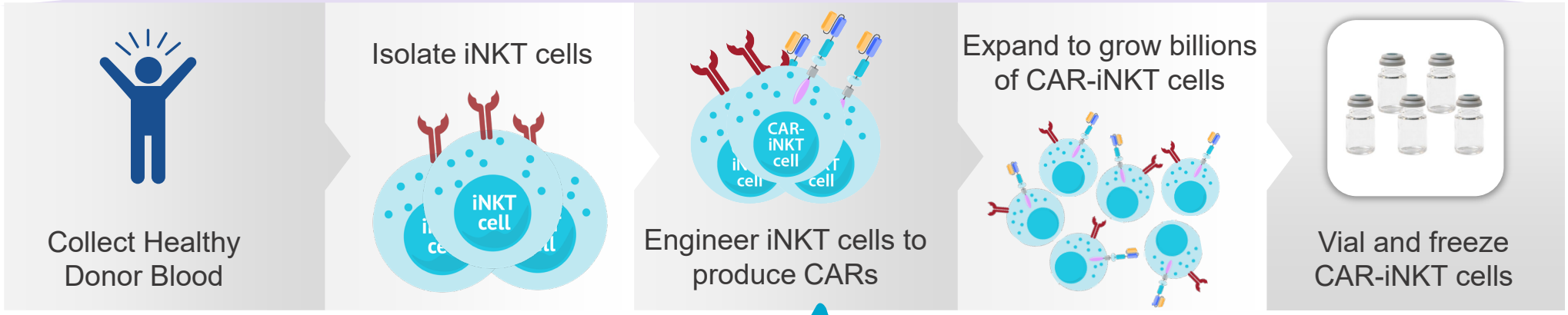



Rotolo *et al.*, Cancer Cell (2018)

# Clinic-ready manufacturing process developed

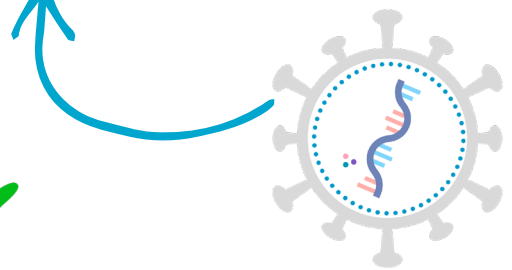
## Semi-automated process suitable for large-scale and late-phase clinical development

TECHNOLOGY ACQUISITION → PRE-CLINICAL CONFIRMATION → LENTIVIRUS MANUFACTURING → **MANUFACTURING PLATFORM** → FDA (IND) / TGA (CTA) → PHASE 1 CLINICAL TRIAL → PHASE 2 CLINICAL TRIAL




**Completed process development with excellent results:**

- **High yield**, >5,000-fold expansion of CAR-iNKT cells
- **>60% of the cells have the CAR (i.e. CAR-iNKT cells)**
- **>99% purity** of iNKT cells
- **Maintains healthy balance** of CD4- and CD4+ cells
- **Semi-automated**, suitable for **large-scale production**
- Potential to leverage **FDA Platform Designation**



**Lentivirus for any CAR**

Completed GMP manufacture of ALA-101 lentivirus

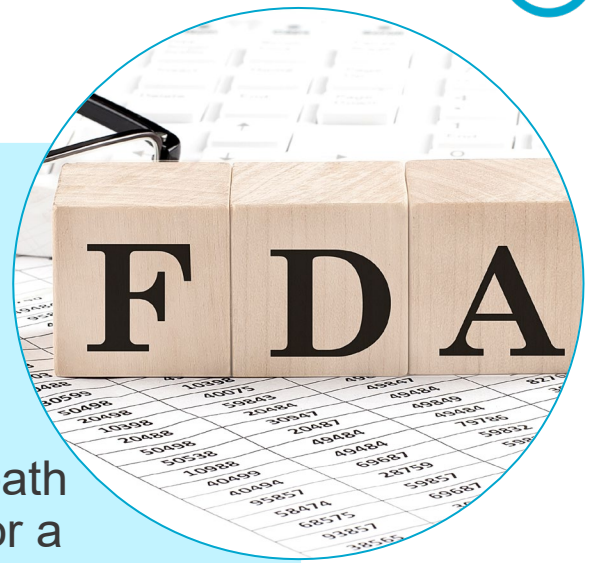
# Successful pre-IND meeting with FDA

ALA is progressing towards its phase 1 study for ALA-101

## First formal interaction with FDA

**Included a review of:**

- Chemistry, Manufacturing and Controls (CMC) data
- Plan for non-clinical safety and efficacy studies
- Proposed phase 1 trial design

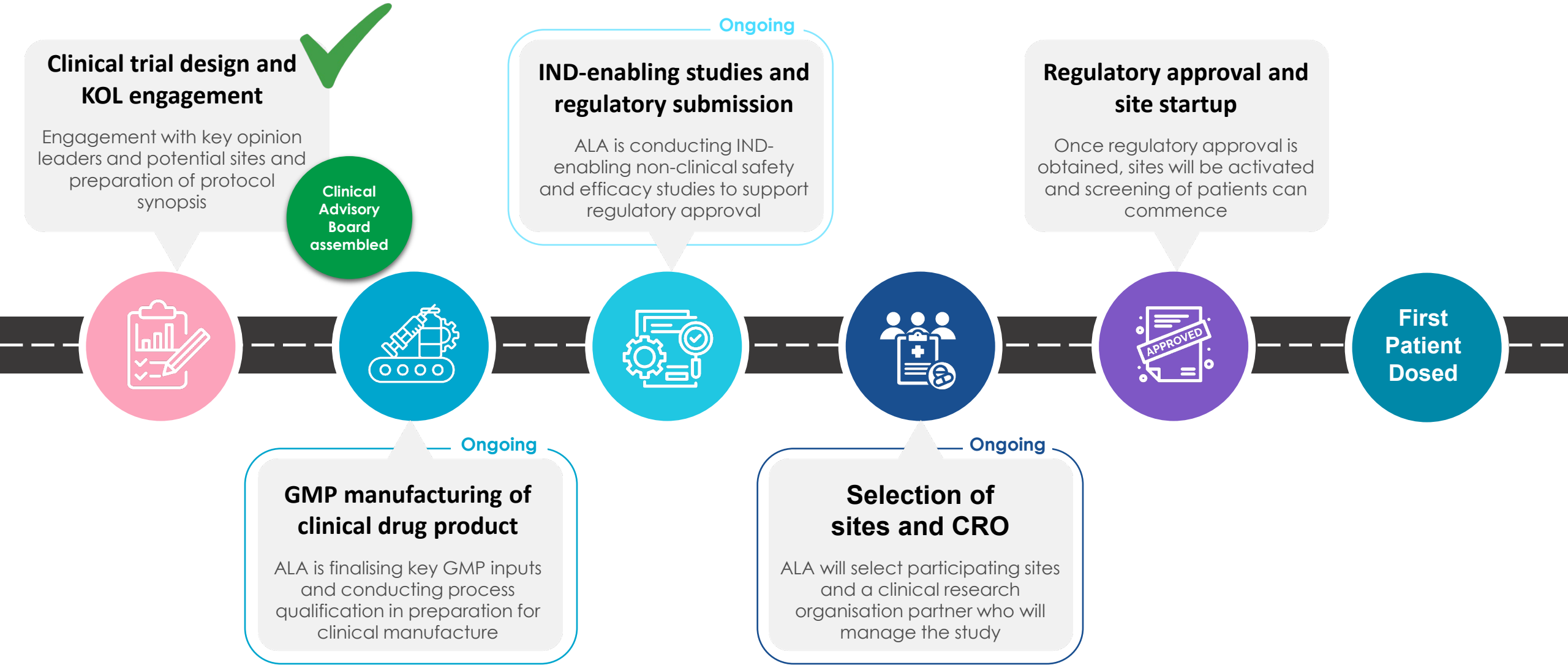



**Positive feedback** and clear path forward to submitting an IND for a phase 1 first-in-human clinical trial for ALA-101

**No major changes** to the development plan proposed by ALA

# Taking ALA-101 into first-in-human trials

## ALA is progressing towards its ALA-101-001 phase 1 study






***Abbreviations***: *CRO, Clinical Research Organization; GMP, Good Manufacturing Practice; IND, Investigational New Drug Application; KOL, Key Opinion Leader*

# Introducing Arovella's Clinical Advisory Board (CAB)

## World class medical oncologists with early phase clinical trial expertise

Dr Salvatore (Sam) Fiorenza

**Epworth HealthCare, Melbourne Australia**

- Dr Fiorenza (MBBS, PhD, BSc (Hons), MPH, FRACP, FRCPA) is a Consultant Haematologist, Deputy Director and Medical Lead of Cellular Therapies at Epworth Healthcare, Melbourne.
- Dr Fiorenza is recognised for his expertise in the development and application of CAR-T cell therapies.

Dr Debora Barton

**ANIM8 LLC**

- Dr Barton, MD, is a highly regarded oncologist with a significant focus on cell therapies.
- Dr Barton has extensive experience designing and running clinical trials from first-in-human phase 1 through to phase 3.

Professor Sattva Neelapu

**The University of Texas MD Anderson Cancer Center, Texas, USA**

- Dr Neelapu, MD, is a Professor and Deputy Chair in the Department of Lymphoma and Myeloma at The University of Texas MD Anderson Cancer Center, Houston, Texas, USA.
- Dr Neelapu is internationally recognised for his pioneering contributions to the development of immunotherapies for blood cancers, particularly in CAR-T therapies.

# ALA-101-001: phase 1 first-in-human study

## Dose escalation and dose expansion study in patients with CD19+ blood cancers

Patients with relapsed or refractory CD19+ non-Hodgkin's lymphoma (NHL, including DLBCL, FL, MCL, MZL) and CD19+ leukemias (including B-ALL, CLL and HCL).

- Single dose of ALA-101 following lymphodepletion regimen
- **Primary objectives**
  - To evaluate the safety and tolerability of ALA-101 in adult patients with CD19+ NHL or leukemia
- **Secondary objectives**
  - To determine the most appropriate dose of ALA-101 for phase 2 clinical trials for adult patients with CD19+ NHL or leukemia
  - To evaluate the preliminary efficacy of ALA-101
  - To characterise the pharmacokinetic (PK) profile of ALA-101

**Part 1: Dose Escalation**

- 4 dose levels
- ~9-12 patients
- CD19+ NHL and leukemias

**Part 2 (phase 1b): Dose Expansion**

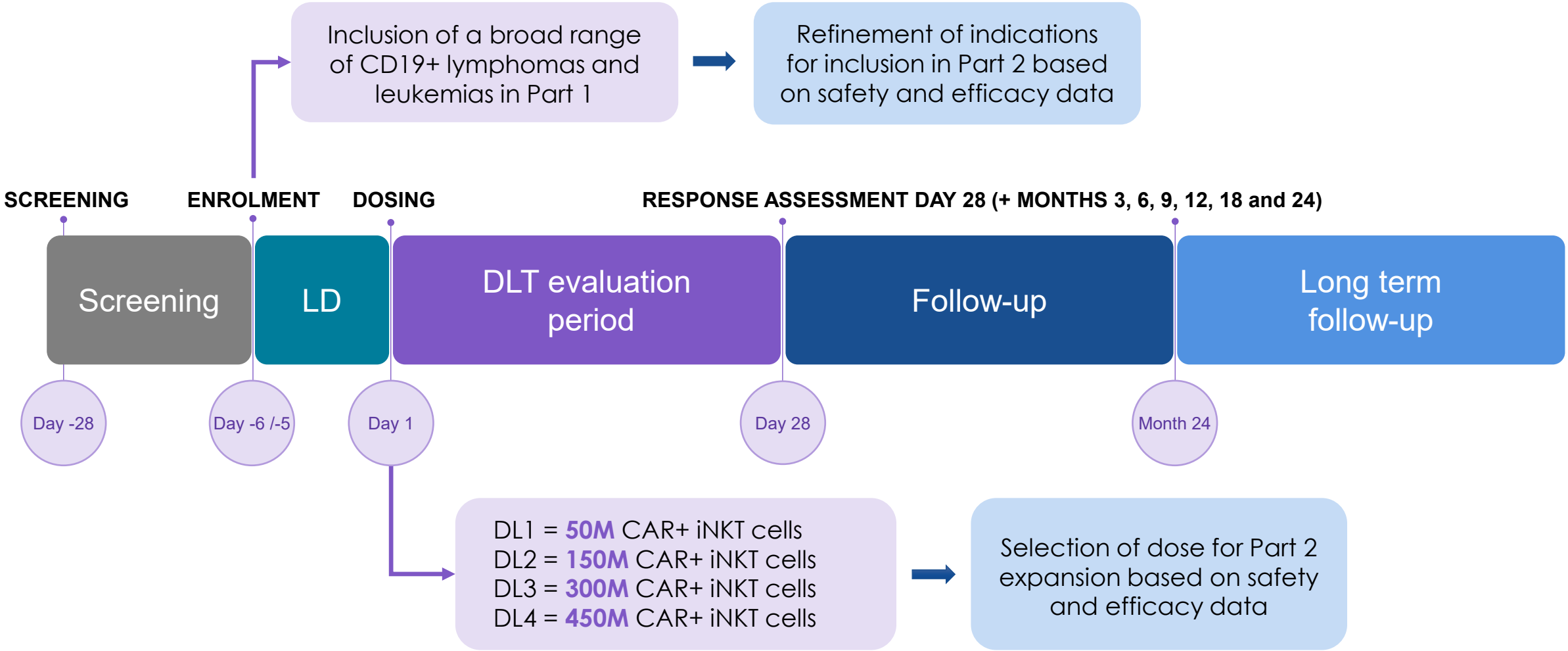
- Dose level selected from Part 1
- ~20 patients
- Sub-indications selected from Part 1

ASX:ALA

***Abbreviations***: *NHL, non-Hodgkin's lymphoma; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; B-ALL, B-cell acute lymphoblastic leukemia; CLL, chronic lymphocytic leukemia; HCL, hairy cell leukemia*

# ALA-101-001: phase 1 first-in-human study

## Anticipated study design




***Abbreviations**: LD, lymphodepletion; DLT, dose limiting toxicities, DL, dose level; CAR, chimeric antigen receptor*

# iNKT cells to target solid tumours

Arovella is implementing its strategy to target and kill solid tumours – 90% of newly diagnosed cancer cases[1]

1. *https://www.cancer.gov/types/common-cancers*

# Arovella's strategies to combat solid tumours

Arovella is using three approaches to expand the iNKT cell platform into solid tumours

## License novel cancer targets

Identify and license new targets that are expressed in multiple cancers to incorporate into Arovella's iNKT cell therapy platform

## Armour iNKT cells

Enhance the performance of iNKT cells by equipping iNKT cells with novel armouring technologies

## Create unique partnerships

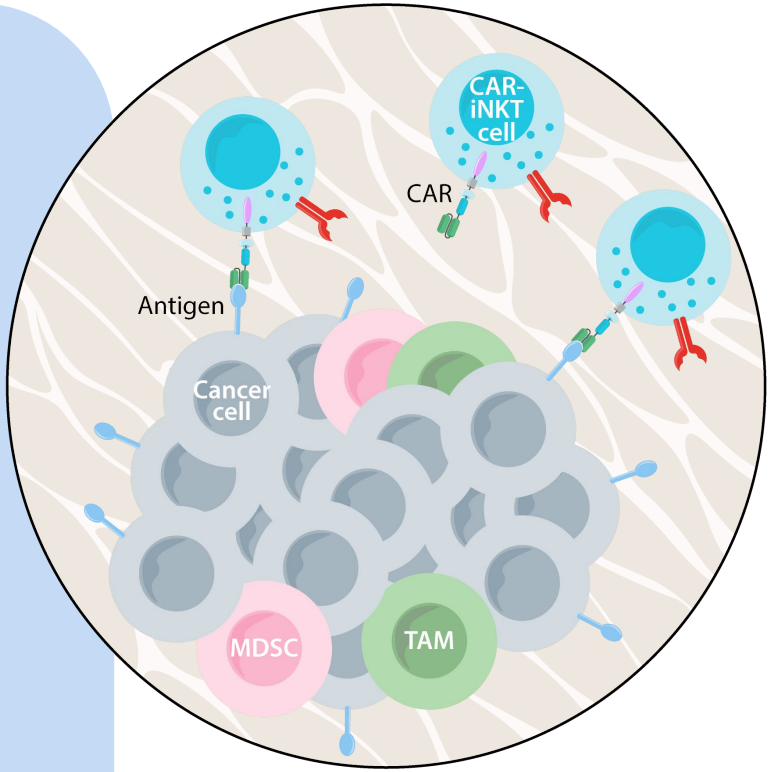
Create partnerships to use novel combination therapies with synergistic effects

# Solid tumours pose challenges to cell therapies

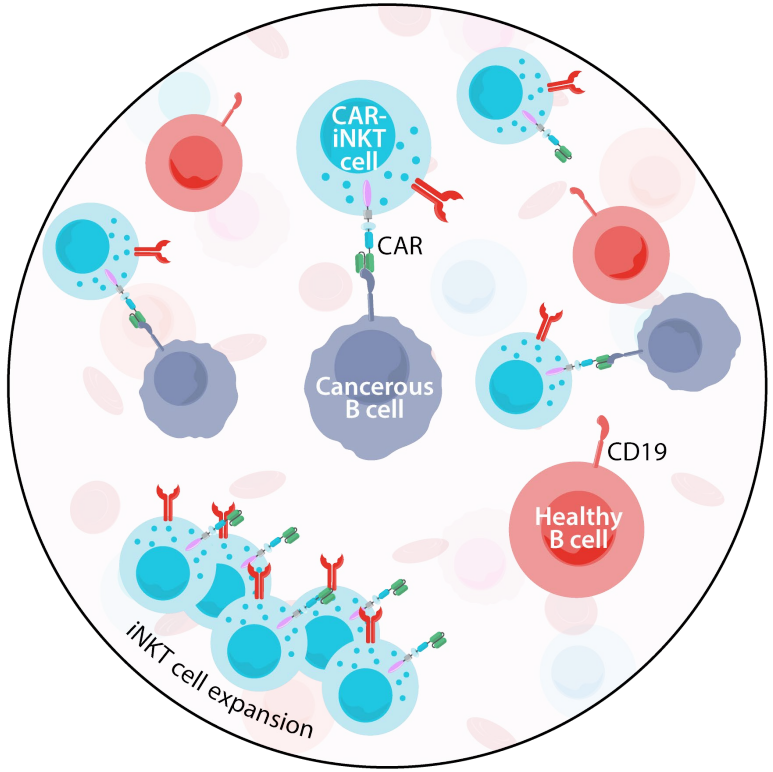
Solid tumours are more

**difficult to treat with cell therapies**

- Access to tumour
- Lack of antigen specificity and uniformity
- Tumour microenvironment contains cells that support cancer cell growth




Solid tumour




Blood cancer

**iNKT cells:**

- Home to tissues and infiltrate tumours
- Modify the TME to block or kill cells that promote tumour growth and recruit helpful immune cells

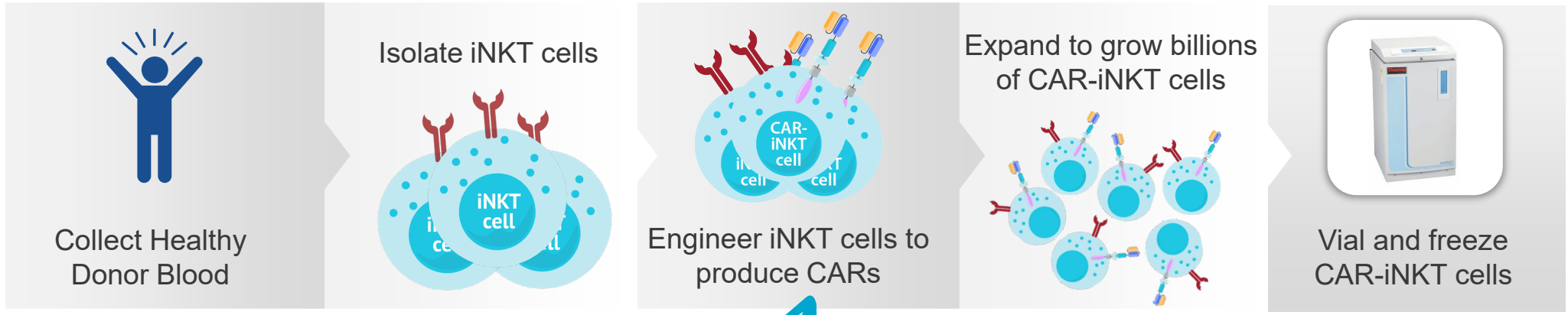
*TAM = Tumour Associated Macrophage; MDSC = Myeloid Derived Suppressor Cell; CAR = Chimeric Antigen Receptor*

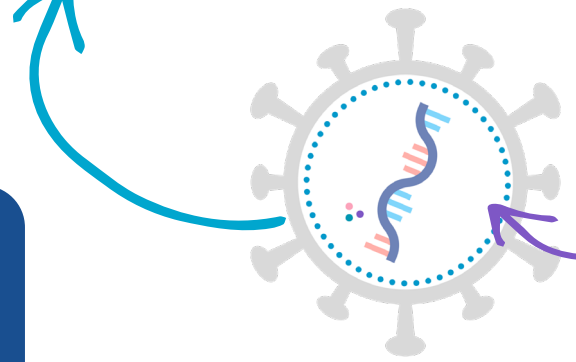
# Add additional CARs for novel targets

New CARs

## Arovella's manufacturing process can be leveraged for multiple cancer types

MANUFACTURING



**New CAR genetic material – e.g. CLDN18.2, IL-12-TM and others**

Arovella has a clinic-ready manufacturing process to manufacture CAR-iNKT cells

**which can be leveraged to create many CAR-iNKT** cell products to target multiple cancer types

**New lentivirus** generated for each new CAR

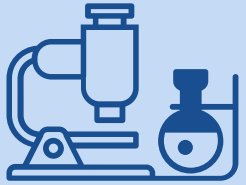
# Introducing Claudin 18.2 (CLDN18.2)

## A promising solid tumour target

CLDN18.2 overexpression has been

**identified in several types of cancers**

- gastric cancer **(GC)**
- gastroesophageal junction cancer **(GEJC)**
- pancreatic cancer **(PC)**
- esophageal cancer **(EC)**
- ovarian adenocarcinoma **(OAC)**
- lung cancers **(LC)**



**Validated target**

with first monoclonal antibody **approved in Japan in 2024**


**Gastric cancer**

market alone expected to reach **$10.7 billion** by 2031[1]

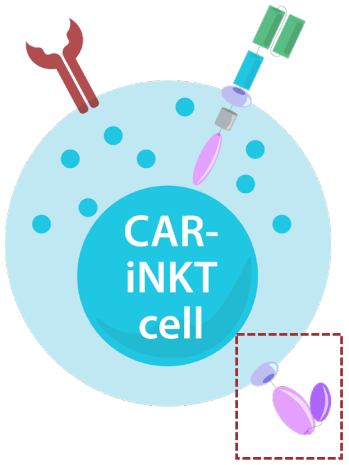
1. *https://www.alliedmarketresearch.com/gastric-cancer-market-A74458#:~:text=The%20global%20gastric%20cancer%20market,cells%20lining%20of%20the%20stomach*

# “Armouring” CAR-iNKT cells

Armouring

## IL-12-TM (cytokine technology) enhances CAR-iNKT cell activity in solid tumours

## IL-12-TM




**IL-12-TM is a modified version of IL-12**

with a membrane anchor that links it to the surface of CAR-iNKT cells. By linking it to the surface of iNKT cells, it can enhance CAR-iNKT cells without being released into the blood stream, making it safer.

The IL-12-TM is incorporated into the lentiviral vector and system and **does not require changes to the manufacturing process**

## iNKT cells + IL-12-TM

**Expand more and survive for longer**
than CAR-iNKT cells lacking the cytokine

**10x more circulating CAR-iNKT cells**
4 weeks after treatment in a mouse model

**Superior anti-tumour activity**
compared to CAR-iNKT cells lacking the cytokine

The technology has been published in the prestigious, peer reviewed journal **Nature Communications**

nature › nature communications › articles › article

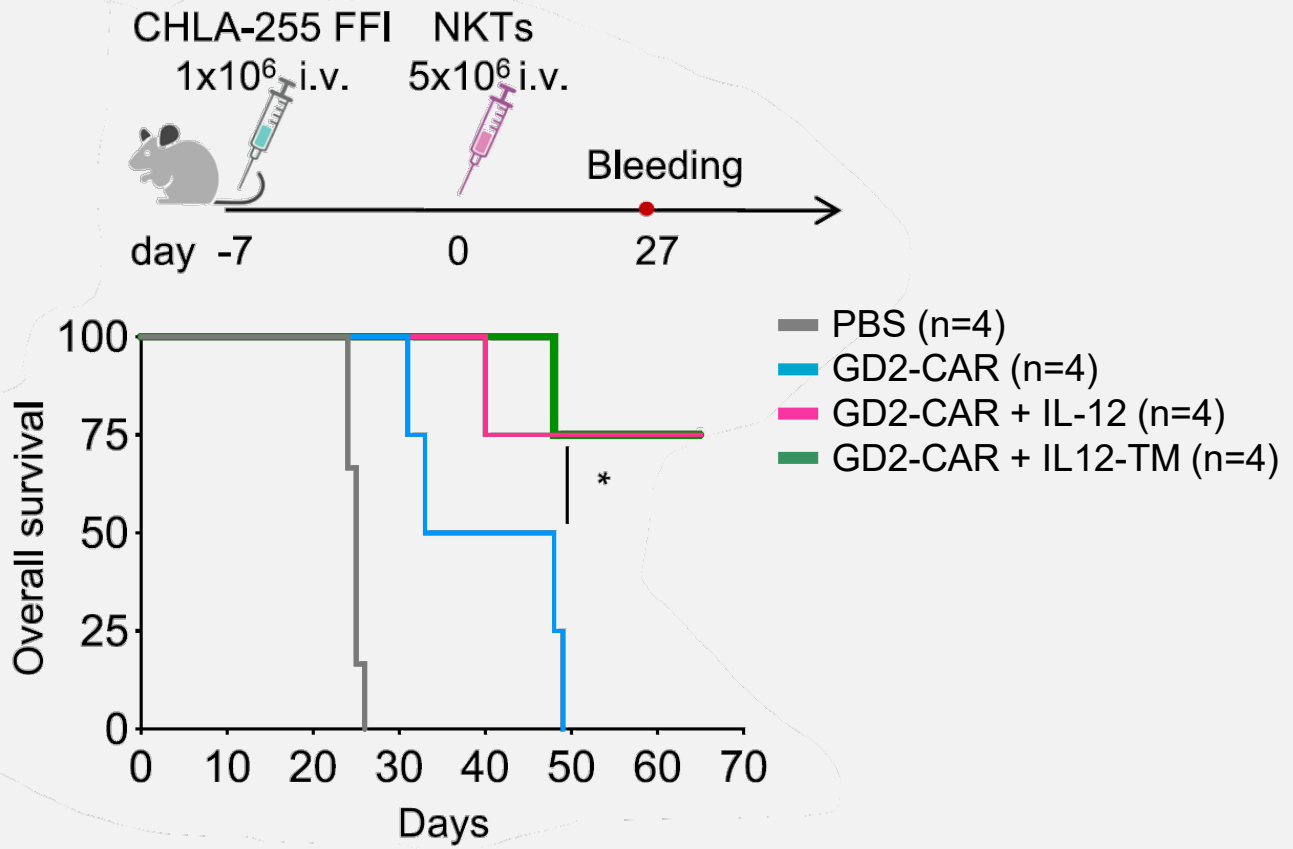
Article | Open access | Published: 02 January 2024

**IL-12 reprograms CAR-expressing natural killer T cells to long-lived Th1-polarized cells with potent antitumor activity**

# Key benefits of IL-12-TM for CAR-iNKT cells

## IL-12-TM enhances antitumor activity of CAR-iNKT cells

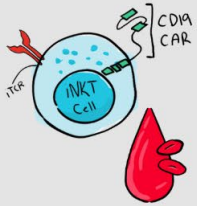
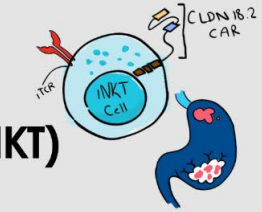
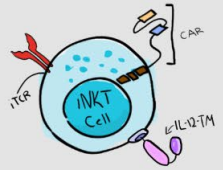
- Tumour cells positive for GD2 and were intravenously delivered into mice before treatment with CAR-iNKT cells
- Mice were treated with:
  - PBS (saline)
  - GD2-CAR
  - GD2-CAR + IL-12
  - GD2-CAR + IL-12-TM
- After 60 days, only mice treated with GD2-CAR + IL12 or IL-12-TM remained alive
- IL-12-TM enhances CAR-iNKT cell numbers and antitumour activity




*statistically significant (p=0.0344)

Landoni *et al.*, Nature Communications (2024)

# Arovella's expanding pipeline

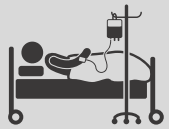
| PRODUCT | INDICATION | DISCOVERY | PRECLINICAL | PHASE 1 |
|---|---|---|---|---|
| **ALA-101 (CAR19-iNKT)**   | CD19-positive cancers | CD19-positive Lymphoma | | |
| **ALA-105 (CLDN18.2-iNKT)**   | CLDN18.2 positive solid tumours | Gastric & Pancreatic Cancers | | |
| **IL-12-TM**   | Solid Tumours | Solid Tumours | | |

# Upcoming milestones for FY2025

July **2024**

July **2025**

| | |
|---|---|
| **ALA-101 (CD19)** | ▪ Complete cGMP manufacture for Phase 1 clinical trials<br>▪ Complete preparatory activities for Phase 1 study, preparation of regulatory dossier, engagement with clinical sites and KOLs<br>▪ Commence phase 1 dose escalation study for ALA-101 in patients with CD19+ NHL and leukemia |
| **ALA-105 (CLDN18.2)** | ▪ Proof-of-concept testing for CLDN18.2-iNKT cells and optimisation of the CAR construct for robust efficacy<br>▪ Generate animal data for CLDN18.2 targeting CAR-iNKT cells against gastric cancer and/or pancreatic cancer<br>▪ Commence activities to manufacture ALA-105 for clinic (e.g. lentiviral vector) |
| **IL-12-TM Integration** | ▪ Integrate IL-12-TM into solid tumour programs and test its efficacy in anti-tumour models<br>▪ Enter into a Sponsored Research Agreement (SRA) with Professor Gianpietro Dotti's research group |
| **Pipeline expansion** | ▪ Continue to identify and acquire novel technologies that enhance and expand Arovella's iNKT cell therapy platform |



**Arovella is funded to dose patients with ALA-101 during FY2025**



***Abbreviations***: *cGMP, current good manufacturing practice; KOLs, key opinion leaders; NHL, non-Hodgkin's lymphoma*

# Summary

## Novel allogeneic CAR-iNKT cell platform

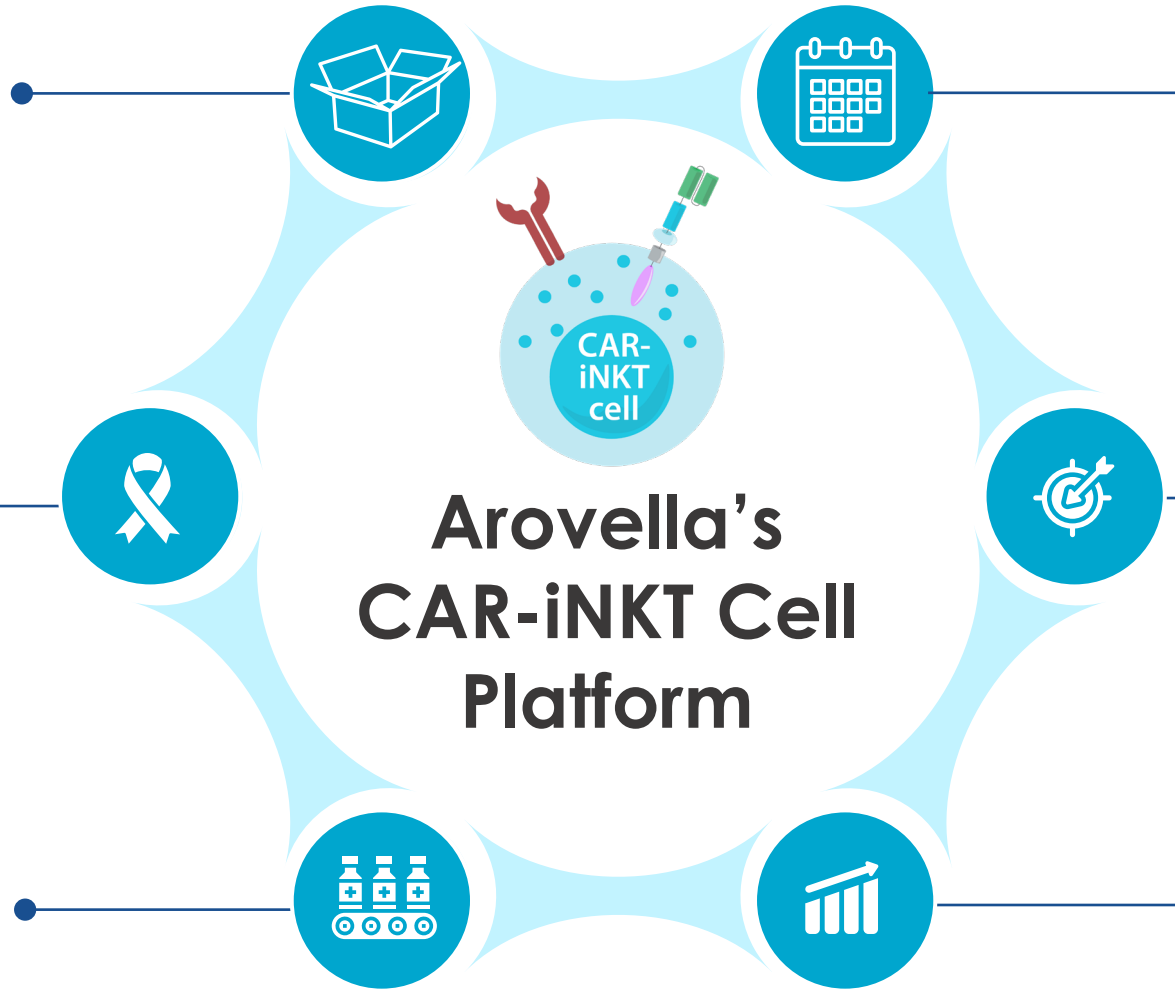
iNKT cells serve as an excellent platform to develop allogeneic, or “off-the-shelf”, cell therapies to treat cancer

## Improved manufacturing logistics

Allogeneic CAR-iNKT cells will significantly improve logistics and increase patient access

## CAR-iNKT cells have multiple anticancer properties

CAR-iNKT cells have multiple anti-cancer properties that may support enhanced efficacy over other immune cell types




## Lead product progressing to clinical trials

ALA-101, a potential treatment for CD19-expressing blood cancers, is being progressed to Phase 1 clinical trials, expected to commence in 2025

## Arovella has an expanding pipeline

Arovella continues to expand the iNKT cell platform with the addition of IL-12-TM armouring and can add different CARs, leveraging its manufacturing process

## Arovella is poised for growth

Arovella is developing a cutting-edge CAR-iNKT cell therapy platform, with an expanding pipeline and a strong leadership team

ASX:**ALA**

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THERAPEUTICS

# Thank You


## Dr. Michael Baker

CEO & Managing Director

Email: investor@arovella.com
Mobile: +61 403 468 187

# Cell therapy deal references


1. https://www.astellas.com/en/news/28271
2. https://www.astrazeneca.com/media-centre/press-releases/2023/astrazeneca-to-acquire-gracell-furthering-cell-therapy-ambition-across-oncology-and-autoimmune-diseases.html
3. https://www.astrazeneca.com/media-centre/press-releases/2023/astrazeneca-cell-and-gene-therapy-deal-w-cellectis.html
4. https://www.businesswire.com/news/home/20230815091930/en/Precision-BioSciences-Completes-Strategic-Transaction-with-Imugene-for-Azer-Cel-in-Cancer
5. https://www.astellas.com/en/news/28271
6. https://www.jnj.com/janssen-enters-worldwide-collaboration-and-license-agreement-with-cellular-biomedicine-group-to-develop-next-generation-car-t-therapies
7. https://www.astrazeneca.com/media-centre/press-releases/2023/acquisition-of-neogene-therapeutics-completed.html
8. https://www.gilead.com/news-and-press/press-room/press-releases/2022/12/kite-and-arcellx-announce-strategic-collaboration-to-co-develop-and-co-commercialize-late-stage-clinical-cart-ddbcma-in-multiple-myeloma
9. https://www.fiercebiotech.com/biotech/genentech-pays-70m-access-arsenals-armoury-t-cell-tools-quest-solid-tumor-car-t
10. https://www.prnewswire.com/news-releases/poseida-therapeutics-announces-strategic-global-collaboration-with-roche-focused-on-allogeneic-car-t-cell-therapies-for-hematologic-malignancies-301598555.html
11. https://www.adaptimmune.com/investors-and-media/news-center/press-releases/detail/197/adaptimmune-enters-into-a-strategic-collaboration-with
12. https://www.gilead.com/news-and-press/press-room/press-releases/2021/8/kite-and-appia-bio-announce-collaboration-to-research-and-develop-allogeneic-cell-therapies-for-cancer
13. https://www.nasdaq.com/articles/athenex-snaps-up-kuur-therapeutics-for-$185m-street-sees-133.7-upside-2021-05-05
14. https://eternatx.com/news/brooklyn-immunotherapeutics-completes-acquisition-of-eterna-therapeutics/