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ASX Release

19 April 2023

AROVELLA AACR POSTER WEBINAR PRESENTATION

- **Investor webinar to be held 11AM AEST today**
- **Describing new data presented at AACR Annual Meeting demonstrating that ALA-101 confers significant anti-tumour effect and survival benefit in aggressive leukemia model**

MELBOURNE, AUSTRALIA 19 April 2023: Arovella Therapeutics Ltd (ASX: ALA) is pleased to provide the presentation to be delivered at its webinar scheduled for today at 11:00 AM (AEST).

The webinar will be an opportunity to hear about the new data that was recently presented by Arovella at the American Association of Cancer Research Annual Meeting in Orlando, Florida. The data demonstrates that ALA-101 confers significant anti-tumour effect and survival benefit in mice with aggressive human B-Cell Acute Lymphoblastic Leukemia (B-ALL) and confirmed that confirmed that the proposed manufacturing process maintained the effectiveness of cryopreserved ALA-101 when used 'off-the-shelf' and after thawing. Arovella's Senior VP of Development and Translational Medicine, Dr Mini Bharathan, will present alongside CEO and MD, Dr Michael Baker.

Shareholders, investors and other interested parties are invited to register and attend via the following link. Further details on how to attend will be provided by email following registration.

https://us02web.zoom.us/webinar/register/WN_uF1SlhqXSvO0ra9_C4qr-g

A recording of the webinar will be made available via the Company's website and social media channels following the event.

Questions can be submitted during the webinar or sent in advance to investor@arovella.com.

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

Dr Michael Baker
Chief Executive Officer & Managing Director
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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 is also expanding its DKK1-peptide targeting technology licenced from MD Anderson and used in conjunction with its iNKT cell therapy platform. 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 α-GalCer 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. For more information, visit www.arovella.com

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.

The Company is also commercialising ZolpiMist™ to treat short-term insomnia.

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 actions of third parties and financial terms. These factors and assumptions are based upon currently available information and the forward-looking statements contained herein speak only as 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; 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.

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ASX:ALA

ALA-101 Confers Significant Anti-Tumour Effect and Survival Benefit in Aggressive Leukemia Model

AACR Poster Presentation Webinar

19 April 2023

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New Data Presented at AACR 2023

Key Highlights:

- iNKT cells could be **well expanded**
- ALA-101 **killed tumour cells that express CD19**, including primary patient tumour cells
- ALA-101 **significantly extended the lifespan of mice** with aggressive human B-Cell Acute Lymphoblastic Leukemia (B-ALL)
- Following expansion, ALA-101 cells **retained the ability to multiply further when exposed to tumour cells** that express CD19.
- Once stimulated, ALA-101 cells **express anti-cancer cytokines**

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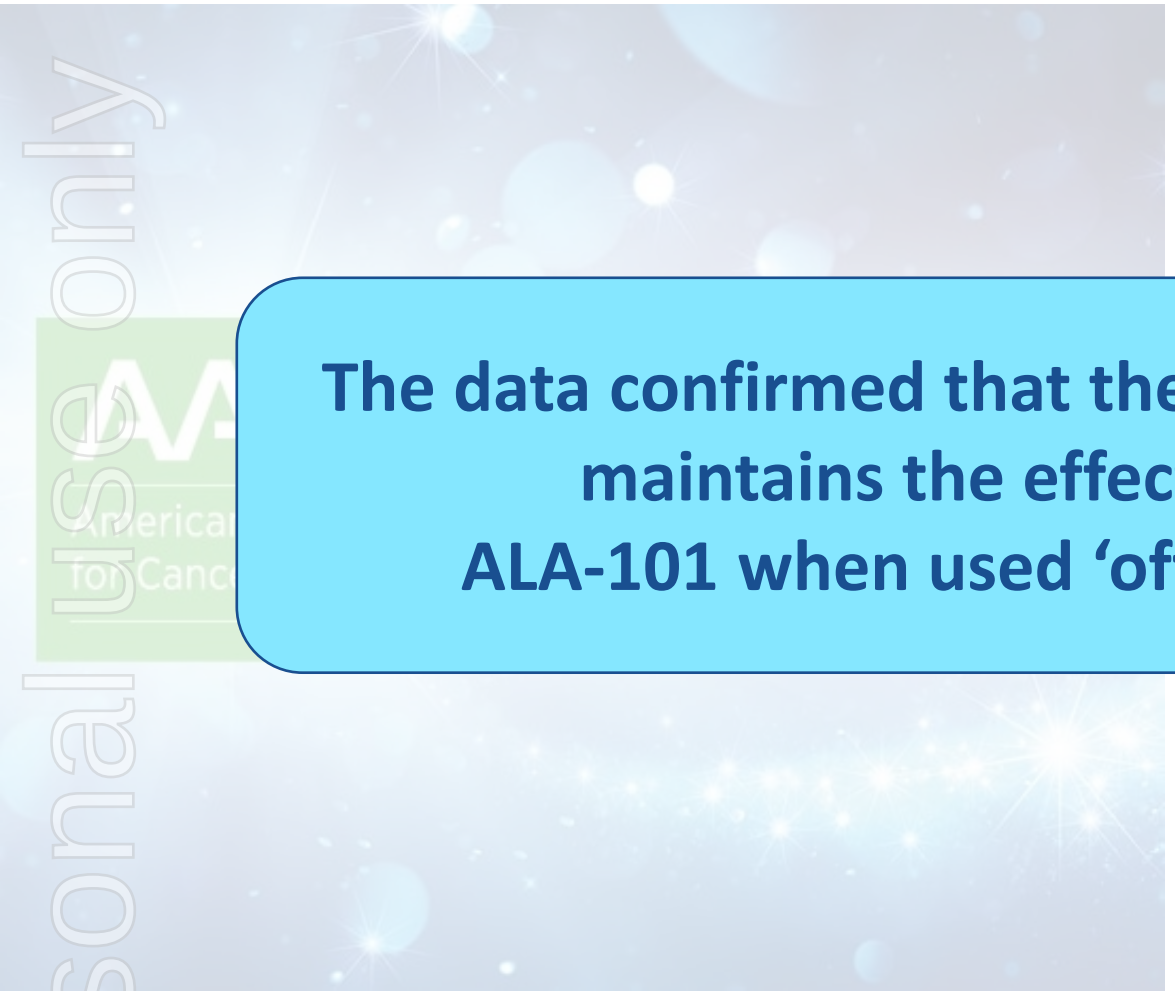
New Data Presented at AACR 2023



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- **tumour**
- **cells** that express CD19.
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The data confirmed that the proposed manufacturing process maintains the effectiveness of cryopreserved ALA-101 when used 'off-the-shelf' and after thawing

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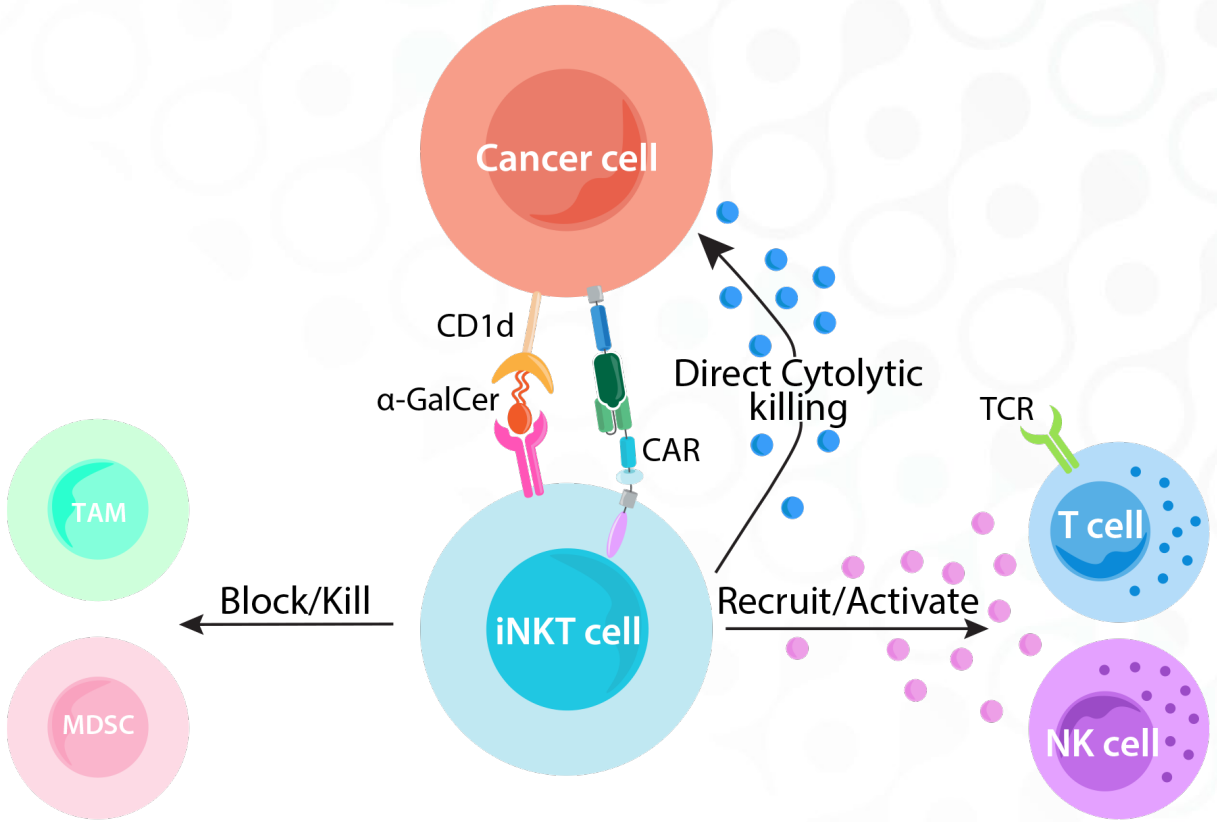
iNKT Cells are Primed to Kill Cancer

- invariant Natural Killer T (iNKT) cells have evolved to target and kill certain cancer cells
- The invariant T Cell Receptor (iTCR) does not change between people so cells from healthy donors can be used and administered “off-the-shelf”
- iNKT cells shape the tumour microenvironment and recruit other components of the immune system to attack cancer cells
- The addition of a Chimeric Antigen Receptor (CAR) makes them dual targeting, enhancing cytotoxicity



TAM = Tumour Associated Macrophage; MDSC = Myeloid Derived Suppressor Cell; CAR = Chimeric Antigen Receptor; NK = Natural Killer

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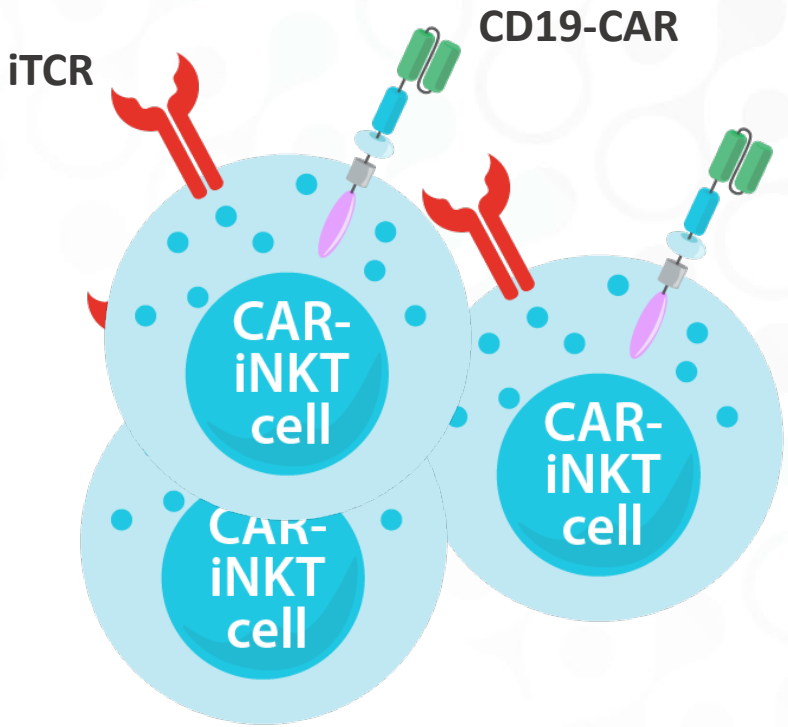
Introducing ALA-101 (CAR19-iNKT Cells)

- Arovella's lead product is ALA-101, a CD19-targeting CAR-iNKT cell therapy
- CD19 is an antigen expressed on normal B cells and malignant B cells of leukemias and lymphomas
  - CD19-targeting CAR T-cells is a proven therapeutic approach for treating lymphoma or B-cell leukemias
- ALA-101 is manufactured using a 3rd-generation lentiviral vector and contains genetic elements with a proven safety profile



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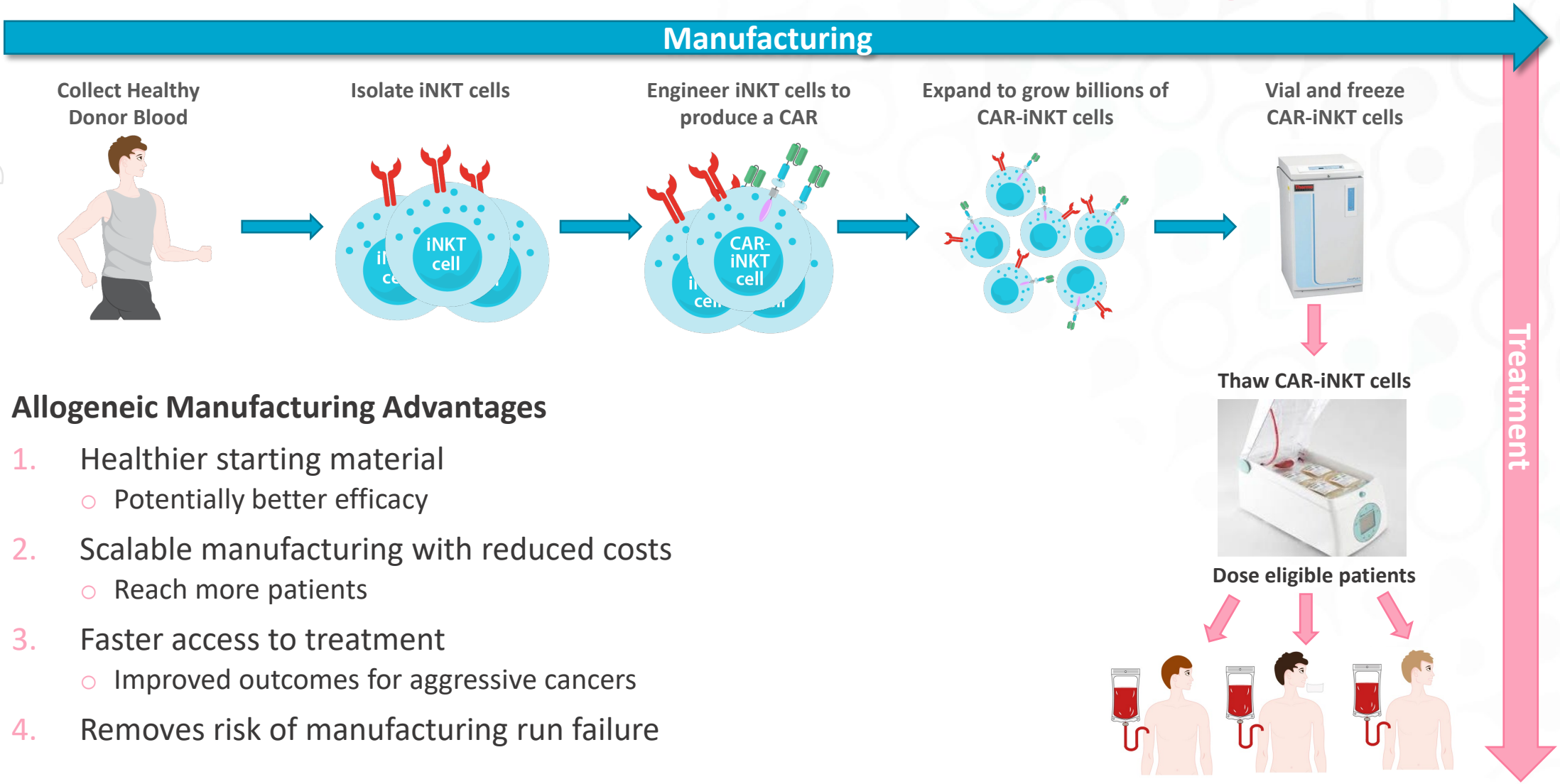
CAR-iNKT Cell Therapy Production Advantages



Allogeneic Manufacturing Advantages

1. Healthier starting material
   - Potentially better efficacy
2. Scalable manufacturing with reduced costs
   - Reach more patients
3. Faster access to treatment
   - Improved outcomes for aggressive cancers
4. Removes risk of manufacturing run failure

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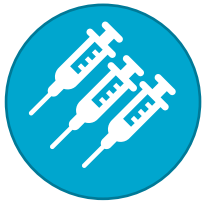
Arovella's iNKT Cell Platform Has Several Advantages

Uses mature iNKT cells from healthy adult donors and does not require 'reprogramming' of stem cells

High 'transduction efficiency', a high percentage of isolated iNKT cells (>60%) become modified to express the CAR

Transduction performed immediately after isolation on low cell numbers, reducing the quantity of expensive reagents required



Efficient expansion of genetically modified cells leads to multiple doses from a single batch

Maintains highly cytotoxic population of iNKT cells

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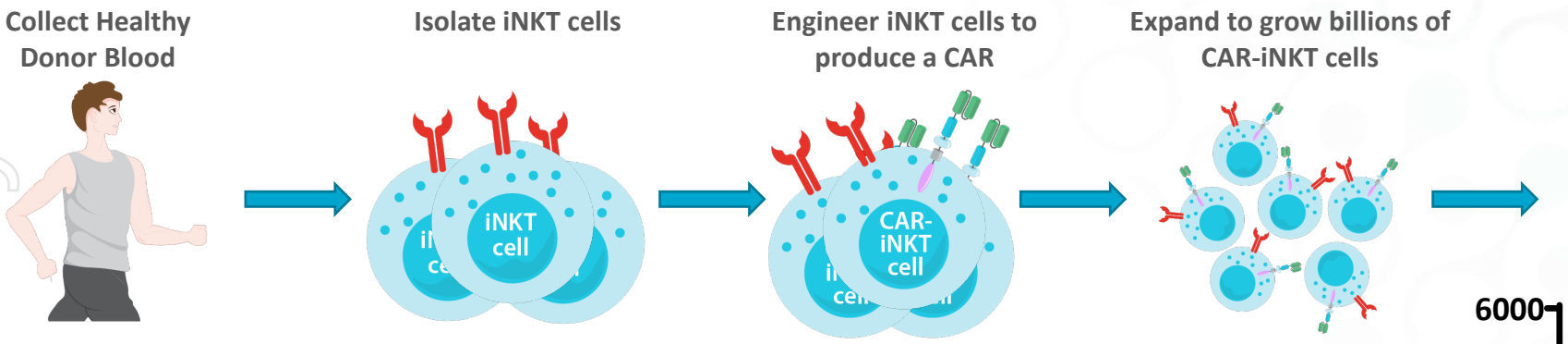
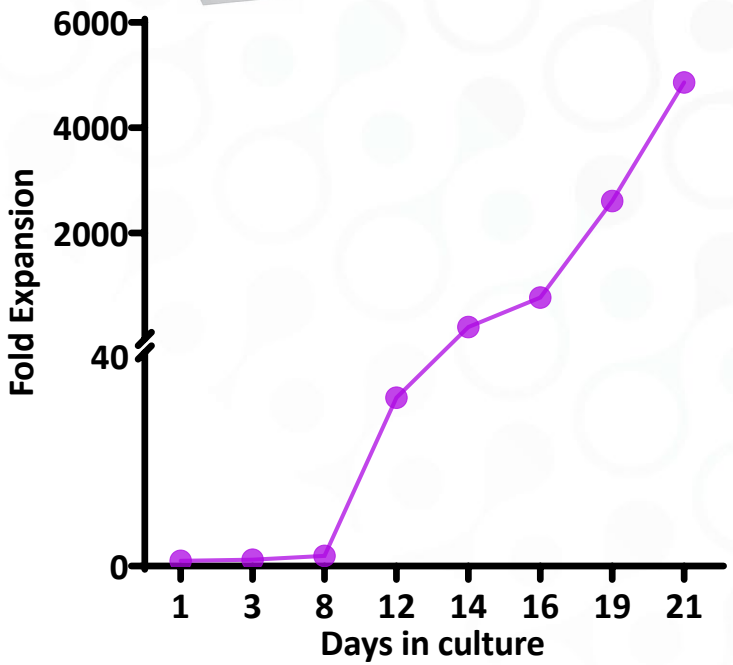
CAR19-iNKT (ALA-101) Cells Can Be Expanded



- iNKT cells from a healthy donor were modified to produce a CD19-targeting CAR using a 3rd generation lentiviral vector from Lentigen Technologies, Inc.

- Cells could be 'expanded' (multiplied) ~5,000-fold to produce large numbers of cells from a single batch
  - Expansion is key to producing an off-the-shelf therapy that addresses the logistical challenges of current autologous cell therapies and provides higher commercial returns through lower manufacturing costs



AACR Poster Fig 2(D)

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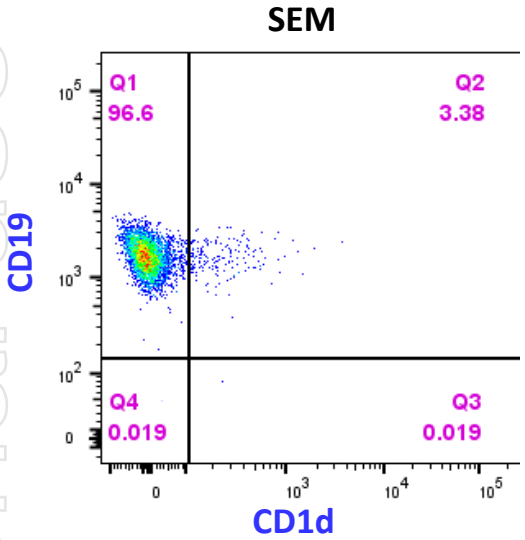
ALA-101 Kills Tumour Cells That Express CD19

- SEM cells originate from a patient with an aggressive form of B-cell Acute Lymphoblastic Leukemia and express CD19, but not CD1d.
- ALA-101 cells efficiently kill multiple leukemia cells lines, including SEM
- ALA-101 eradicated >90% of viable CD19+ cells from a marginal-zone lymphoma patient sample



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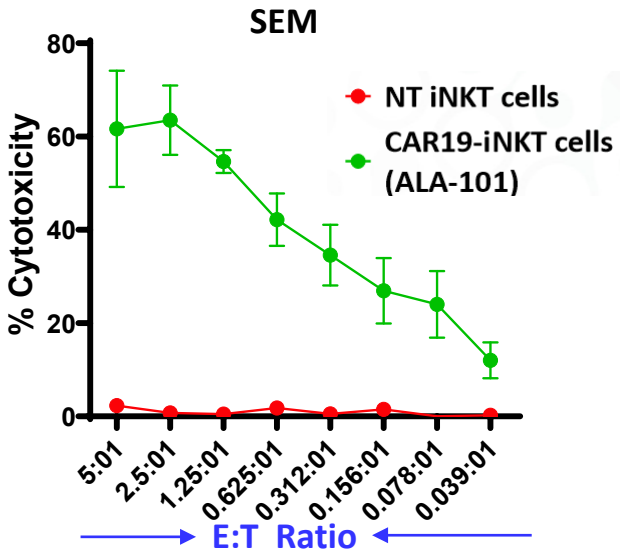
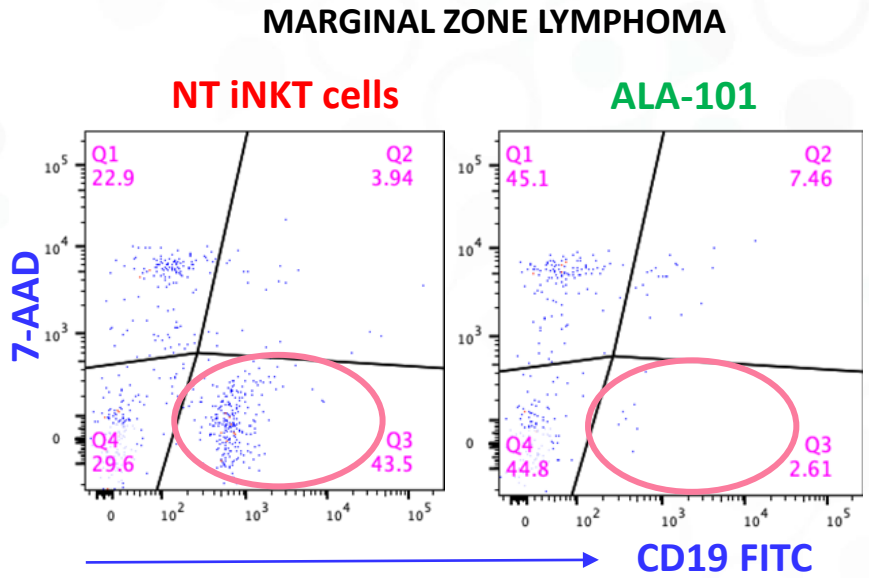


AACR Poster Fig 3(C)



AACR Poster Fig 3(B)

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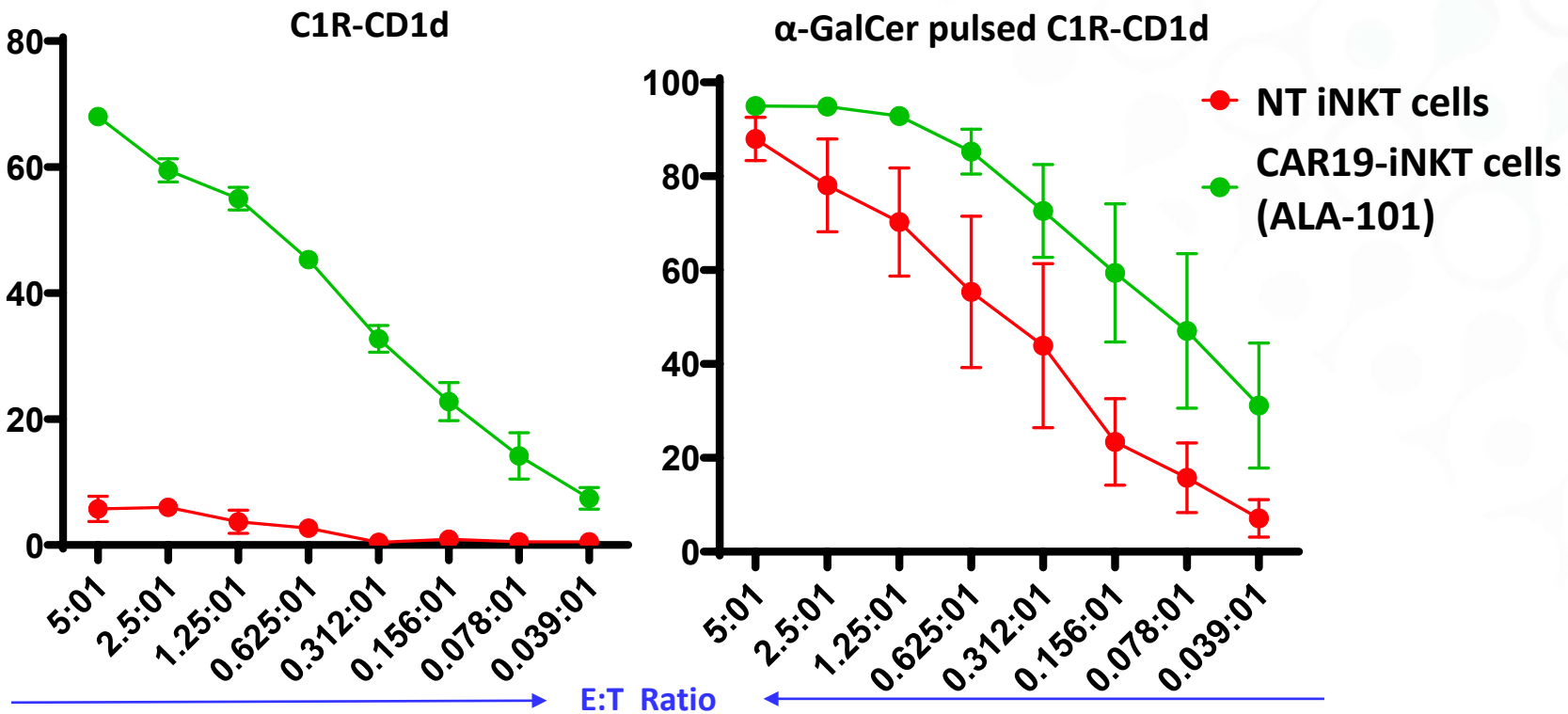
ALA-101 is Dual Targeting

- The dual-targeting potential of ALA-101 was confirmed through efficient killing of C1R-CD1d cells and enhanced killing when these cells were loaded with α-GalCer



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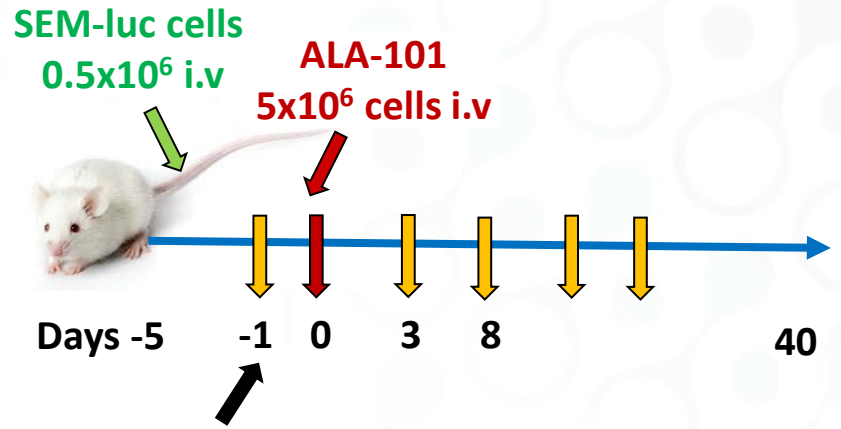
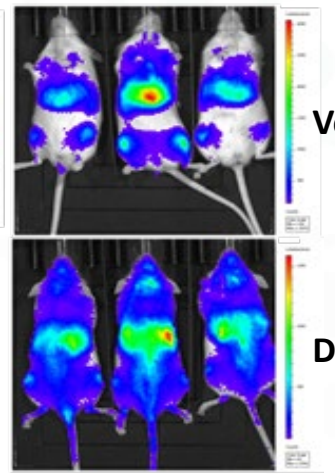
ALA-101 is Effective in an Aggressive Leukemia Model

- ALA-101 was tested in mouse model of B-Cell Acute Lymphoblastic Leukemia (B-ALL) model
- Mice were transplanted with SEM cells originating from a patient with an aggressive form of B-ALL
- After the tumour was established, mice were treated with a relatively low dose of ALA-101





Bioluminescence showing tumour engraftment at Day -1

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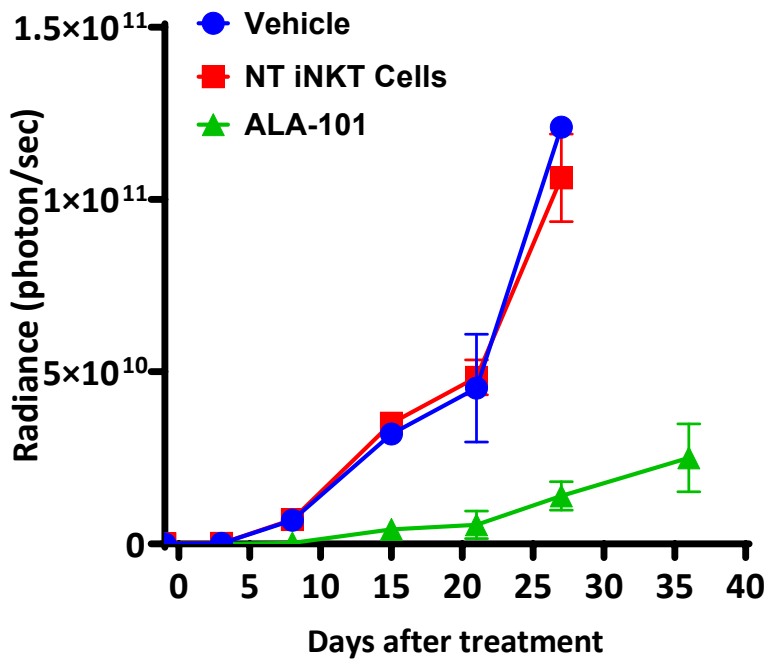
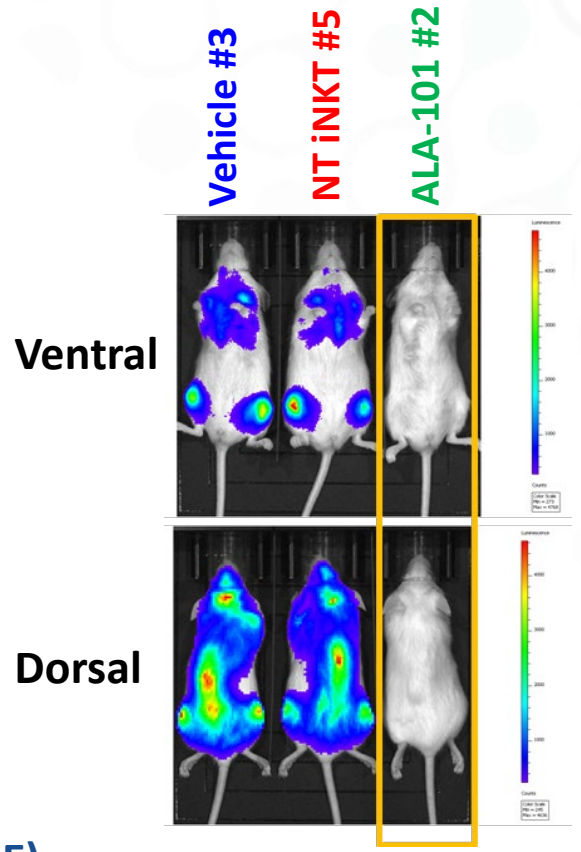
ALA-101 Dramatically Reduced Tumour Burden

- After 26 days, tumour burden in ALA-101-treated mice was ~90% lower than control animals
- Bioluminescent imaging reveals substantially lower tumour burden in ALA-101-treated animals on Day 8





AACR Poster Fig 5(B) & (E)

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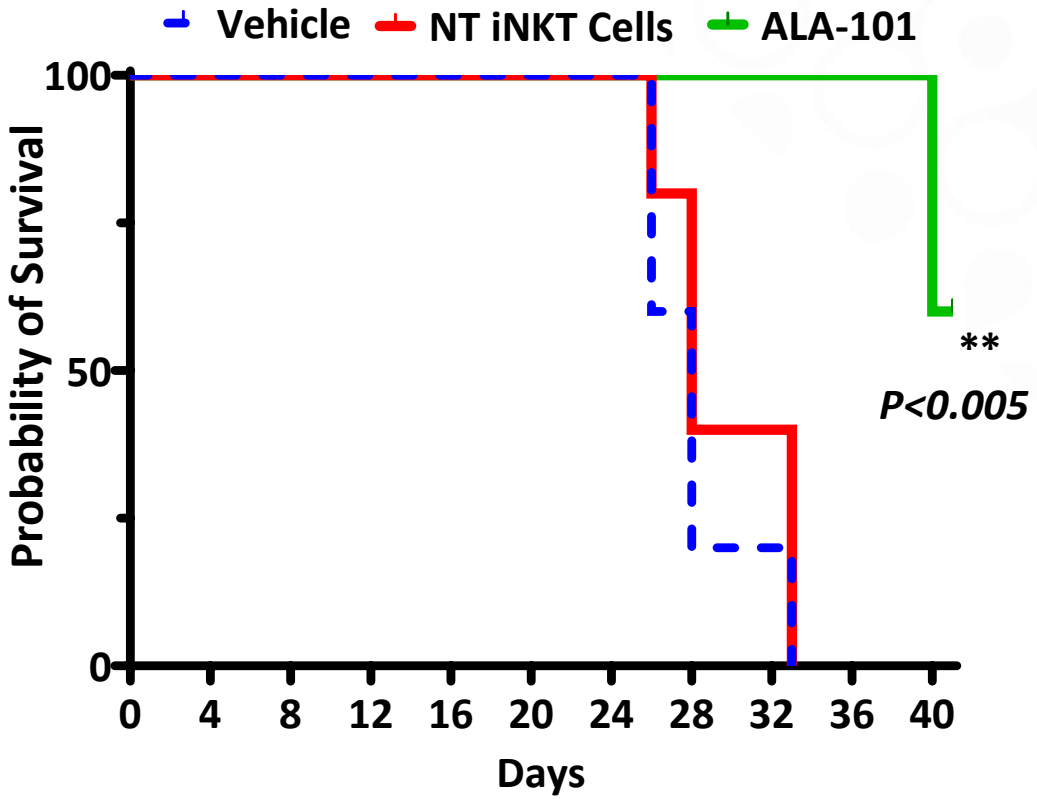
ALA-101 Significantly Increased Animal Survival

- ALA-101 significantly enhanced the survival of the mice over untreated controls (p<0.005)



AACR Poster Fig 5(C)

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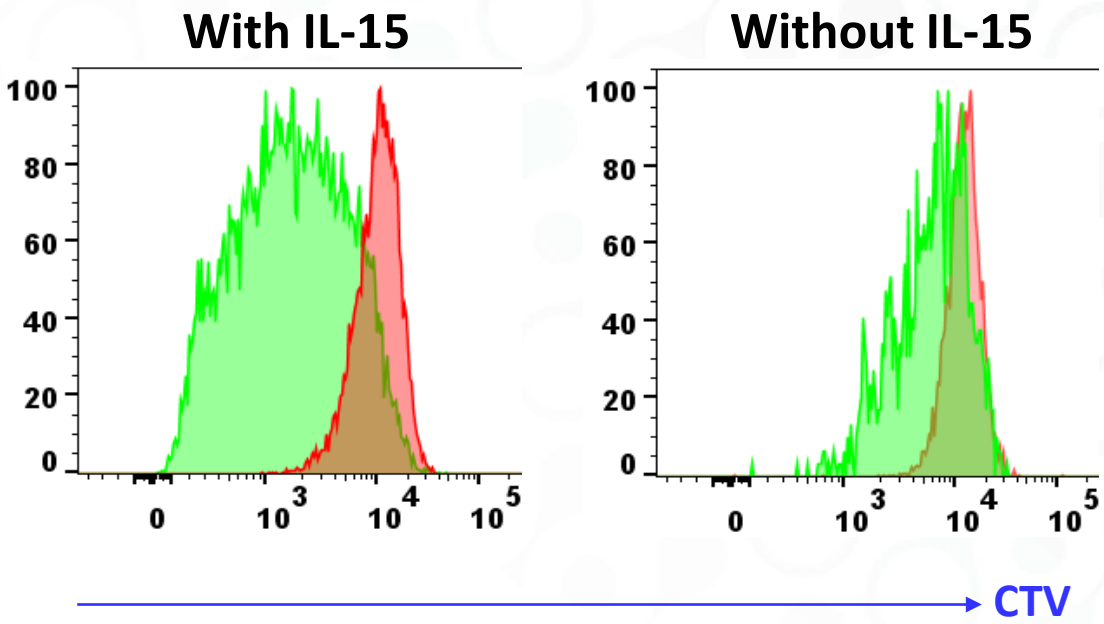
Expanded iNKT Cells Retain the Ability to Proliferate

- ALA-101 cells that had been expanded ~5,000 fold were labeled with a fluorescent dye (CTV)
- Cells were then exposed to SEM tumour cells that were either positive (CD19+) or negative (CD19-) for CD19 expression on their surface
- Upon exposure to CD19+ tumour cells, ALA-101 cells continued to divide and multiply
  - Cell division produces a shift in the signal to the left as a result of decreased CTV levels in the cells
- **This continued expansion is expected to occur in treated patients, enhancing persistence and efficacy**



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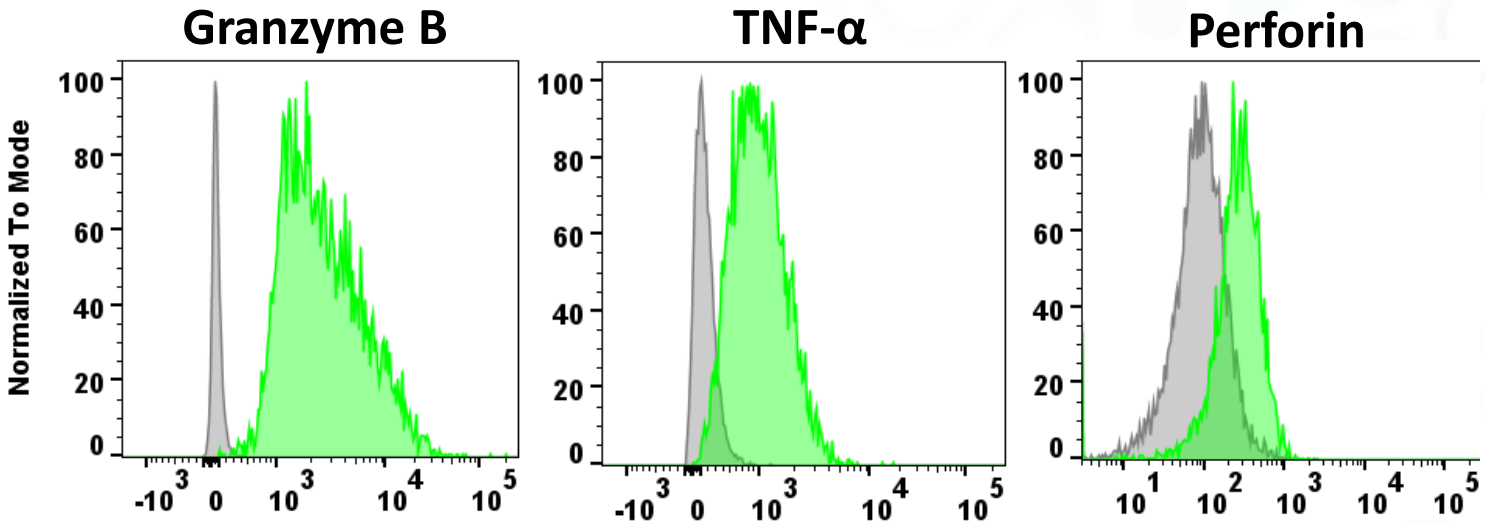
ALA-101 Releases Anti-Tumour Cytokines

- When stimulated by tumour cells expressing CD19, ALA-101 cells dramatically up-regulated the anti-tumour cytokines Granzyme B, TNF-α and Perforin

Unstimulated

Stimulated by CD19+ tumour cells



AACR Poster Fig 4(A)

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Summary

- Arovella's proprietary manufacturing process allows for efficient expansion of iNKT cells while retaining functionality
  - Essential to produce multiple doses from a single batch and address the manufacturing costs and logistical challenges of current autologous therapies

- Arovella has produced ALA-101 using a 3rd-generation lentiviral vector from Lentigen Technologies, Inc., in preparation for the manufacture of clinical material
  - Lentiviral vector and genetic elements with proven safety profile

- ALA-101 conferred significant anti-tumour effect and significantly extended lifespan in an aggressive model of human B-Cell Acute Lymphoblastic Leukemia (B-ALL)
  - Confirming the potential of ALA-101 as an effective treatment for CD19+ leukemias and lymphomas

Arovella continues to progress ALA-101 towards first-in-human clinical trials

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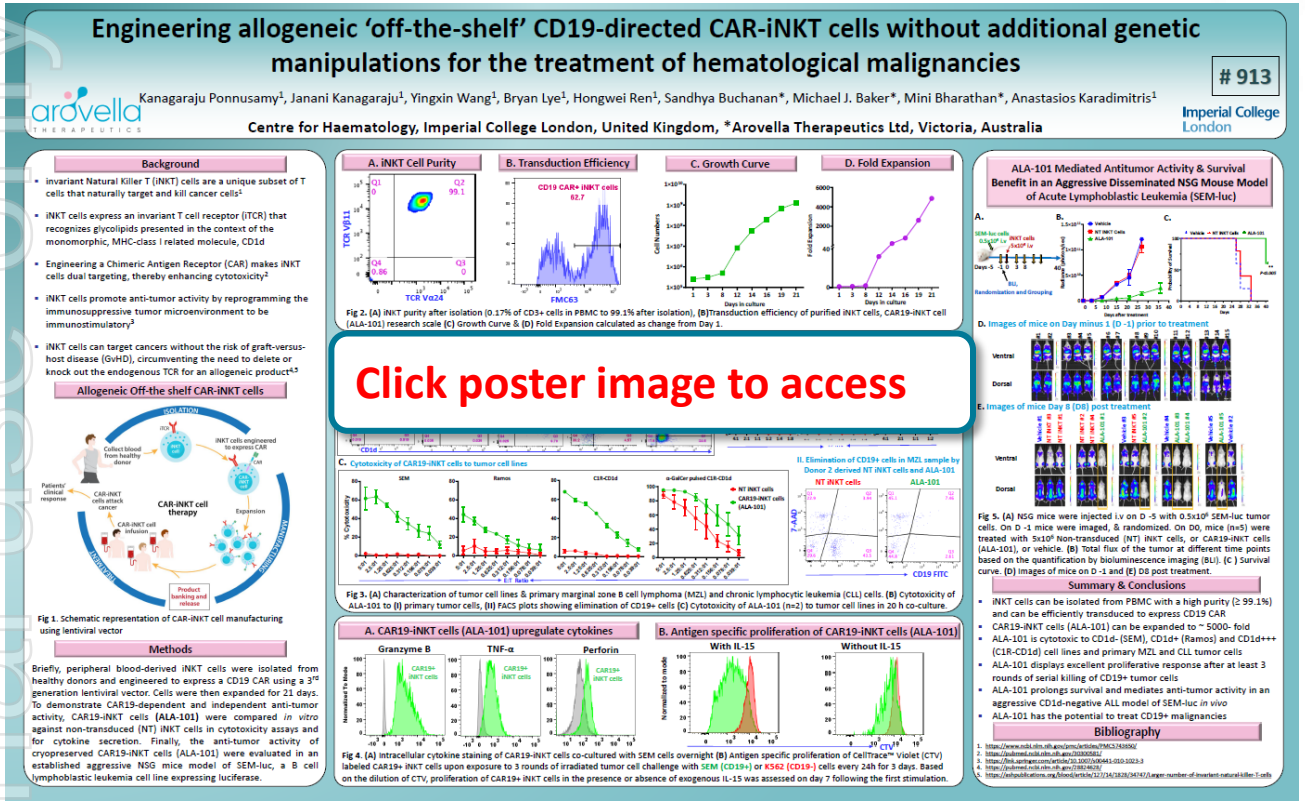

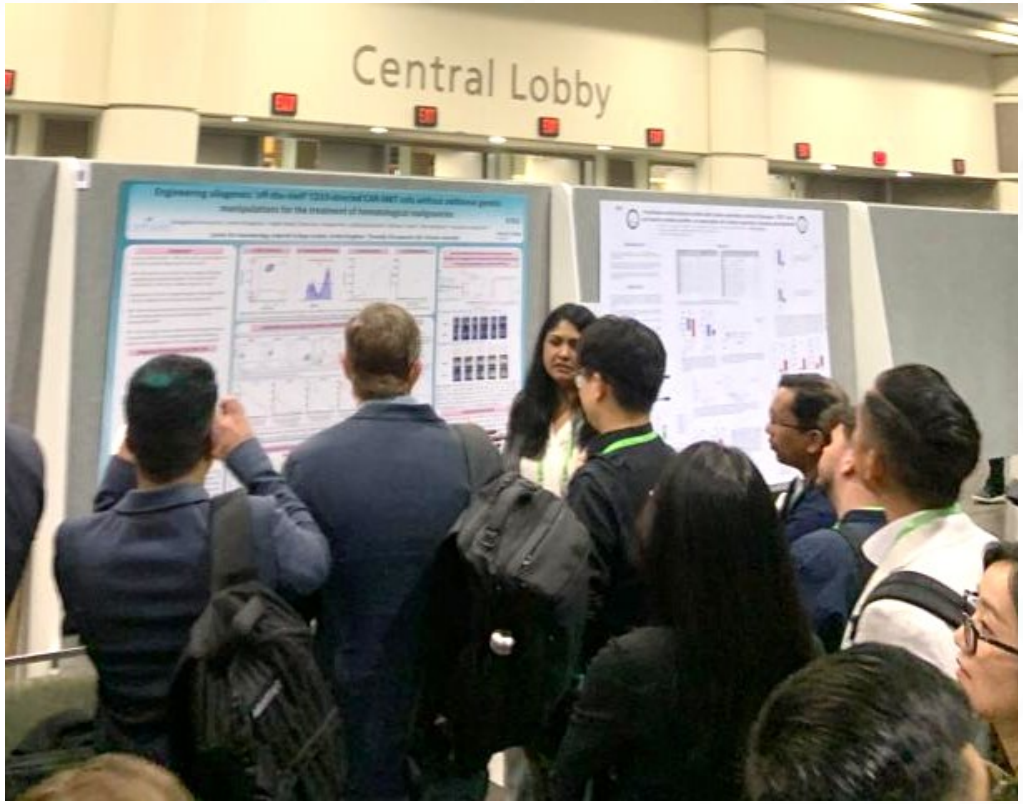

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ALA-101 Scale-Up and Preparation for Clinical Material

Complete ✓

Optimised viral vector to engineer the CAR with regulatory-friendly elements

On track ✓

Identify high-frequency iNKT cell donors

Ongoing H1 2023

Optimise manufacturing process to produce clinical-grade material

Planned H2 2023

Scale-up and and generate data required for regulatory submissions

Produce clinical material

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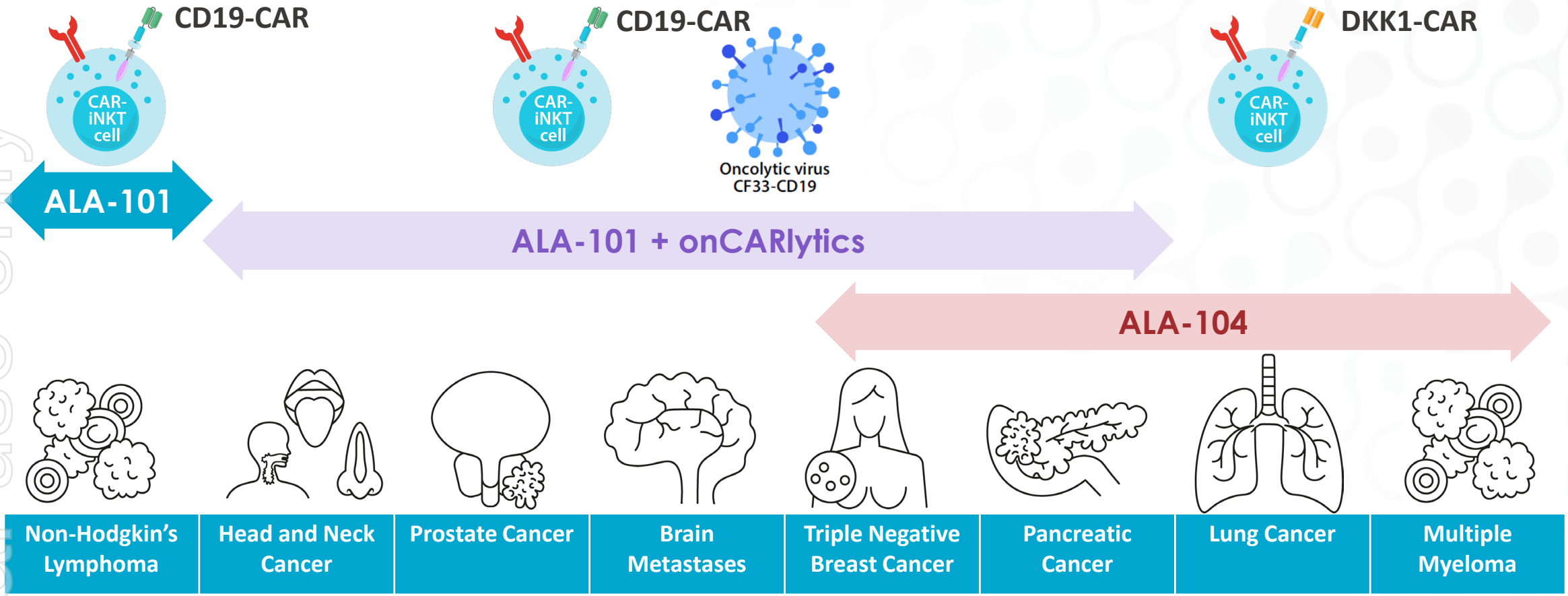
Arovella's Potential Cancer Targets



- Additional CARs can be used to target different cancer types:
  - **Blood Cancers** - CD20, CD22, CD79b; **Solid tumours** – mesothelin, EGFRvIII, IL13α32, GPC3, HEPG2, GD2

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Arovella's Key Milestones Over 18 Months

Cell Therapy

	Partner	Discovery	Lead Optimisation	IND-Enabling	Phase 1
CAR19-iNKT **(ALA-101)**		CD19 Expressing Lymphoma			
ALA-101 + onCARlytics	IMUGENE Developing Cancer Immunotherapies	Solid Tumours			
DKK1-CAR-iNKT **(ALA-104)**		Multiple Myeloma			
		TNBC			
		NSCLC			
		Pancreatic			

TNBC – triple negative breast cancer; NSCLC – non-small cell lung carcinoma

- Over the next 6-18 months Arovella plans to:
  - Complete clinical manufacturing of ALA-101
  - Commence Phase 1 clinical trial with ALA-101 for Non-Hodgkin's Lymphoma
  - Complete proof of concept studies and commence IND-enabling studies for ALA-101 + onCARlytics
  - Complete CAR-optimisation for IND enabling studies for ALA-104

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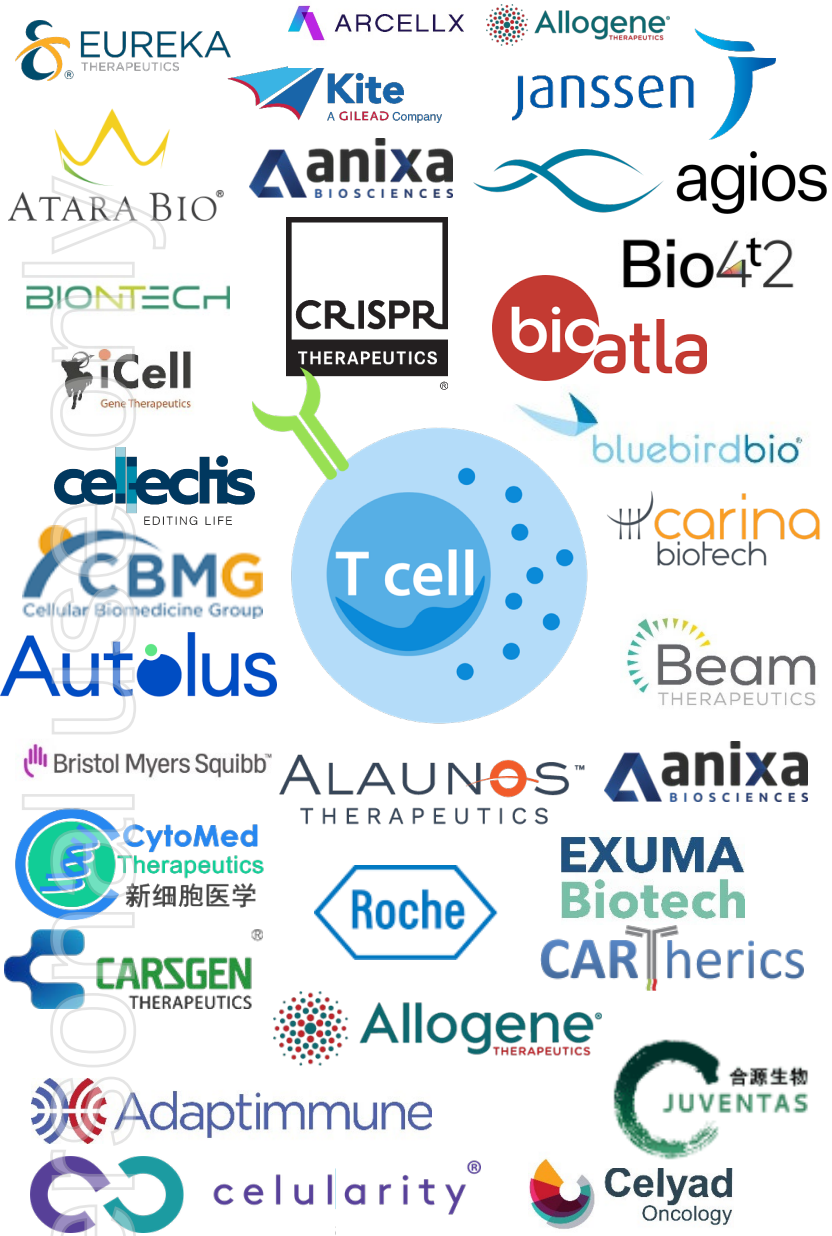
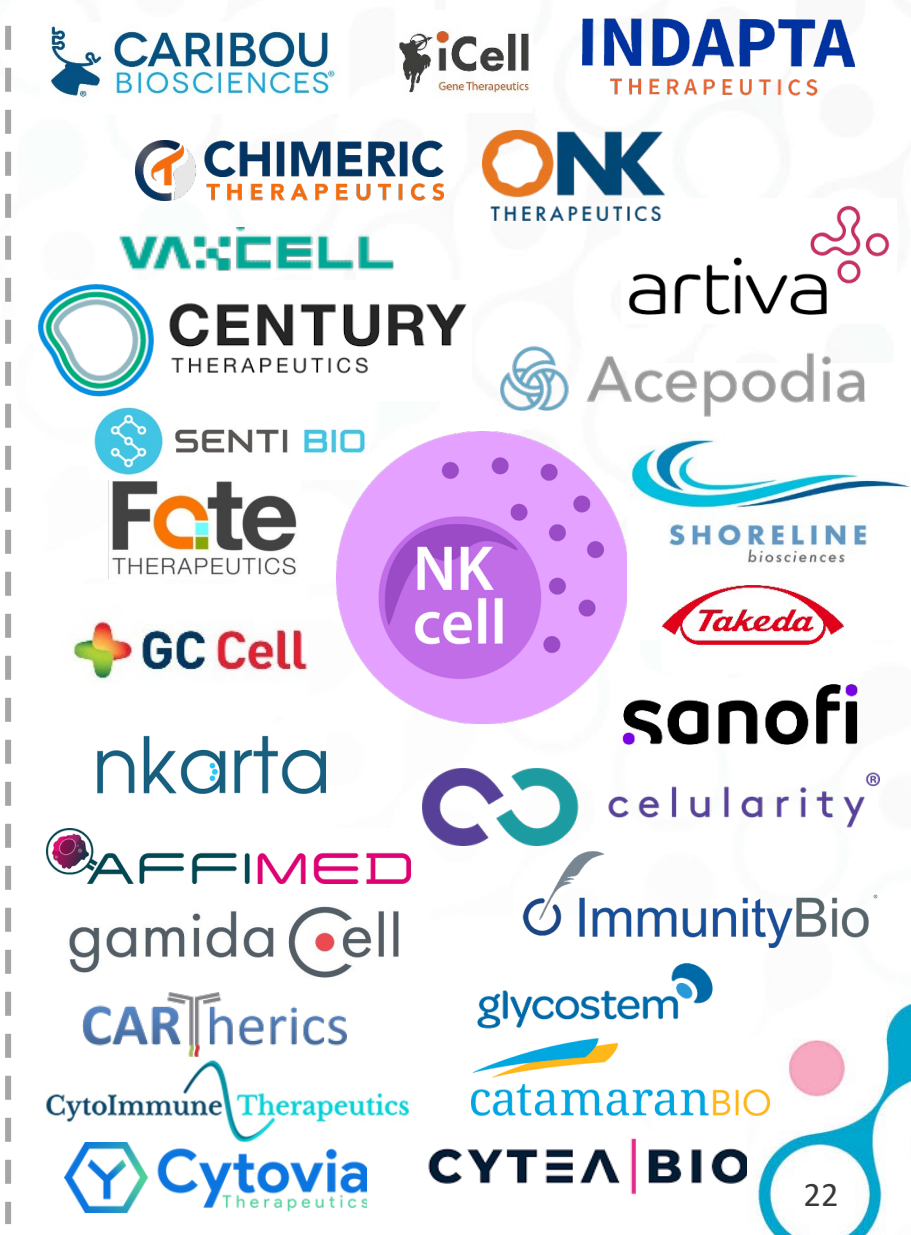
The Potential of CAR-iNKT Cells is Untapped





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

Recent Cell Therapy Transactions

Date	Type of deal	Acquirer/Licensee	Target/Licensor	Stage	Upfront ($M)	Milestones ($M)	Total deal value
Jan-23	Acquisition	AstraZeneca	neogene THERAPEUTICS	Phase I	$200	$120	$320
Oct-22	Development collaboration	GILEAD	ARCELLX	Phase II	$225*	undisclosed	
Sep-22	Research collaboration	Genentech A Member of the Roche Group	ArsenalBio™	Preclincal	$70	undisclosed	
Aug-22	Licence and strategic collaboration	Roche	POSEIDA THERAPEUTICS	Phase I	$110	$110	$220
Sep-21	Development collaboration	Genentech A Member of the Roche Group	Adaptimmune	Preclincal	$150	$150	$300
Aug-21	Research collaboration	GILEAD	APPIA BIO	Preclinical	undisclosed	undisclosed	$875
May-21	Acquisition	Athenex	»kuur THERAPEUTICS	Phase I	$70	$115	$185
Jun-21	Acquisition	eterna	Novellus THERAPEUTICS	Preclinical	$125	$0	$125
Dec-19	Acquisition	astellas	XYPHOS	Preclinical	$120	$545	$665
				Mean	**$134**	**$208**	**$364**

**Arcellx also received a $100m equity investment from Gilead*

Source: Company analysis based on public information

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Arovella Financial Overview

Financial Snapshot

ASX CODE	ALA
Market capitalisation[1]	$61.2 million
Shares on issue	755.5 million
52-week low / high	$0.020 / $0.105
Cash (30 December 2022)[2]	$5.2 million

Major Shareholders

Shareholder	Ownership (%)[1]
THE TRUST COMPANY (AUSTRALIA) LTD	52,796,657 (7.08%)
MANN BEEF PTY LTD	20,000,000 (2.68%)
UBS NOMINEES PTY LTD	15,064,640 (2.02%)
DYLIDE PTY LTD	15,000,000 (2.01%)
FINCLEAR NOMINEES PTY LTD	14,999,571 (2.01%)

1. *As of 18 April 2023*
2. *Includes $1.65m proceeds from the Placement announced 19 January 2023*

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Arovella Has a Strong Leadership Team

Imperial College London

LEADERSHIP

Dr. Michael Baker
CEO & MANAGING DIRECTOR

University of Cologne | The University of Melbourne Melbourne Business School | BioScience Managers

Dr. Nicole van der Weerden
CHIEF OPERATING OFFICER

hexima | The University of Melbourne Melbourne Business School

Dr. Mini Bharathan
SENIOR VP DEVELOPMENT & TRANSLATIONAL MEDICINE

NIH National Cancer Institute | cellectis | Celgene

Dr. Robson Dossa
SENIOR DIRECTOR MANUFACTURING & QUALITY

InstilBio | Kite, A Gilead Company

Ana Radeljevic
BUSINESS DEVELOPMENT

SANOFI genzyme | REPERTOIRE Immune Medicines

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