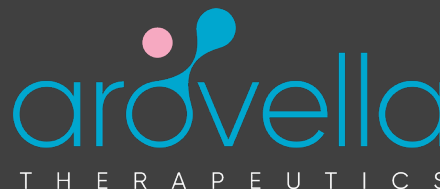


## ASX: ALA

Arovella Therapeutics Limited  
ACN 090 987 250



### 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 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](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](mailto: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**

**Arovella Therapeutics Ltd**

Tel +61 (0) 403 468 187

[investor@arovella.com](mailto:investor@arovella.com)

## ASX: ALA

Arovella Therapeutics Limited  
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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  $\alpha$ -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](http://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;  **$\alpha$ GalCer** – 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.



ASX:ALA

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

**AACR Poster Presentation Webinar**

19 April 2023

# Disclaimer

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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**

# 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**

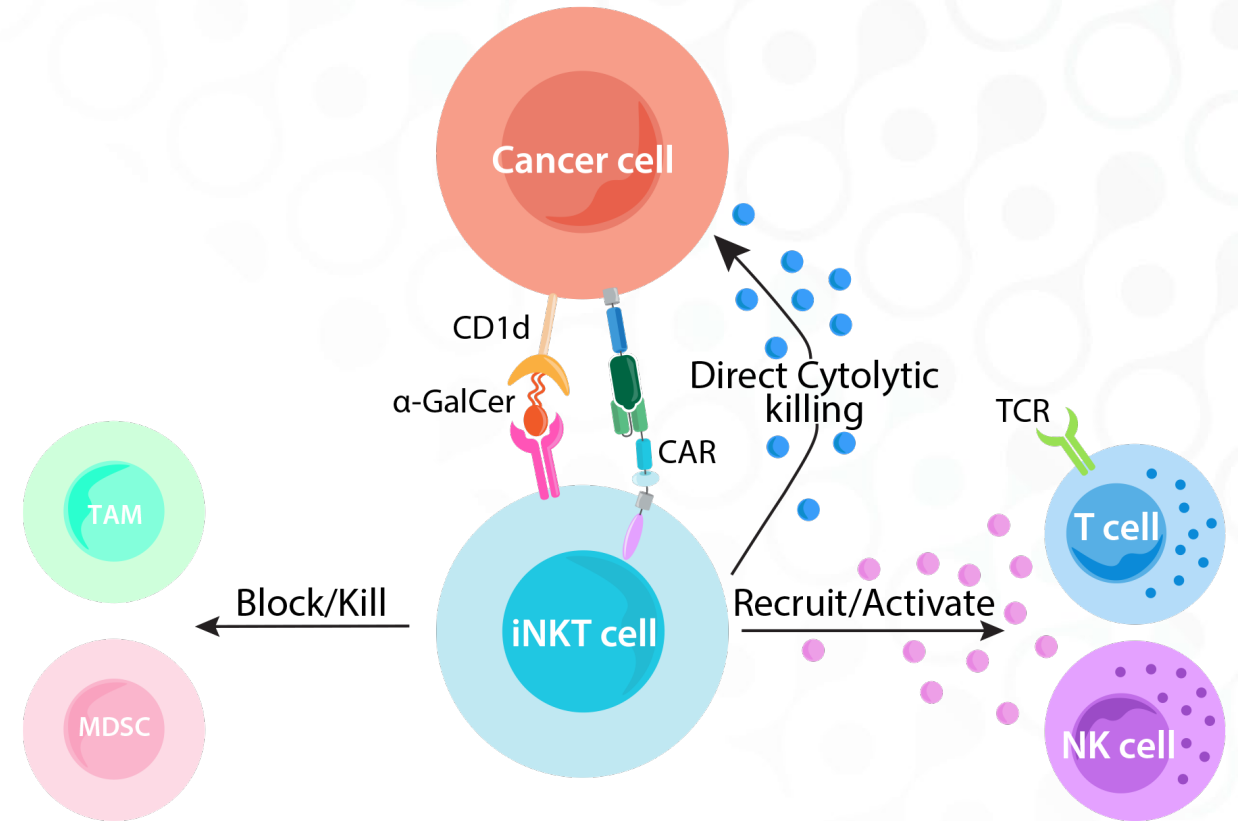
**The data confirmed that the proposed manufacturing process maintains the effectiveness of cryopreserved ALA-101 when used 'off-the-shelf' and after thawing**

**cells that express CD19.**

- Once stimulated, ALA-101 cells **express anti-cancer cytokines**

# iNKT Cells are Primed to Kill Cancer

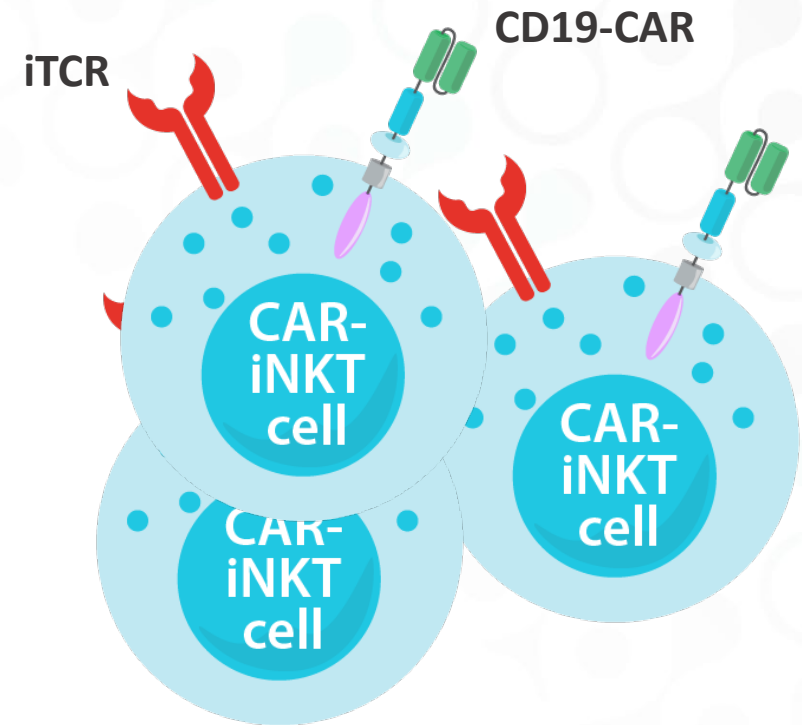
- invariant Natural Killer T (iNKT) cells have evolved to target and kill certain cancer cells
- The invariant T Cell Receptor (iTTCR) does not change between people so cells from healthy donors can be used and administered “off-the-shelf”
- iNKT cells shape the tumour microenvironment and recruit other 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

# Introducing ALA-101 (CAR19-iNKT Cells)

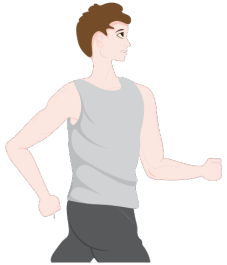
- Arovella's lead product is ALA-101, a CD19-targeting CAR-iNKT cell therapy
- CD19 is an antigen expressed on normal B cells and malignant B cells of leukemias and lymphomas
  - CD19-targeting CAR T-cells is a proven therapeutic approach for treating lymphoma or B-cell leukemias
- ALA-101 is manufactured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



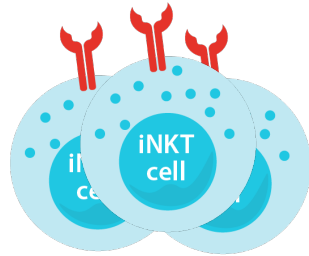
# CAR-iNKT Cell Therapy Production Advantages

## Manufacturing

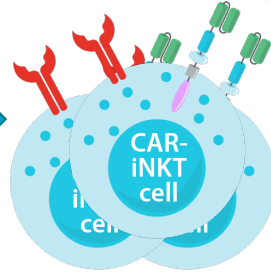
Collect Healthy Donor Blood



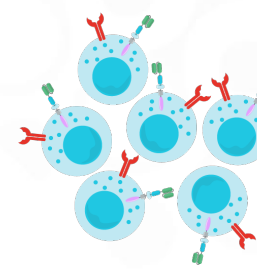
Isolate iNKT cells



Engineer iNKT cells to produce a CAR



Expand to grow billions of CAR-iNKT cells



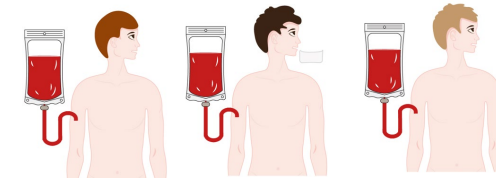
Vial and freeze CAR-iNKT cells



Thaw CAR-iNKT cells



Dose eligible patients



Treatment

## 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

# Arovella's iNKT Cell Platform Has Several Advantages



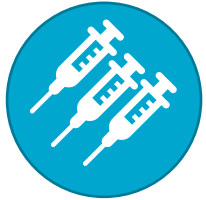
Uses mature iNKT cells from healthy adult donors and does not require 'reprogramming' of stem cells



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



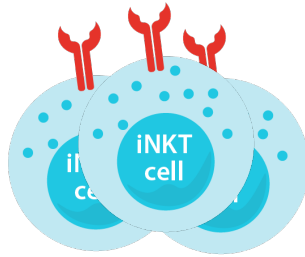
Maintains highly cytotoxic population of iNKT cells

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

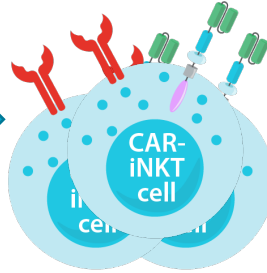
Collect Healthy Donor Blood



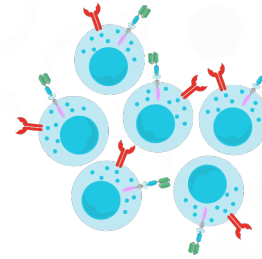
Isolate iNKT cells



Engineer iNKT cells to produce a CAR



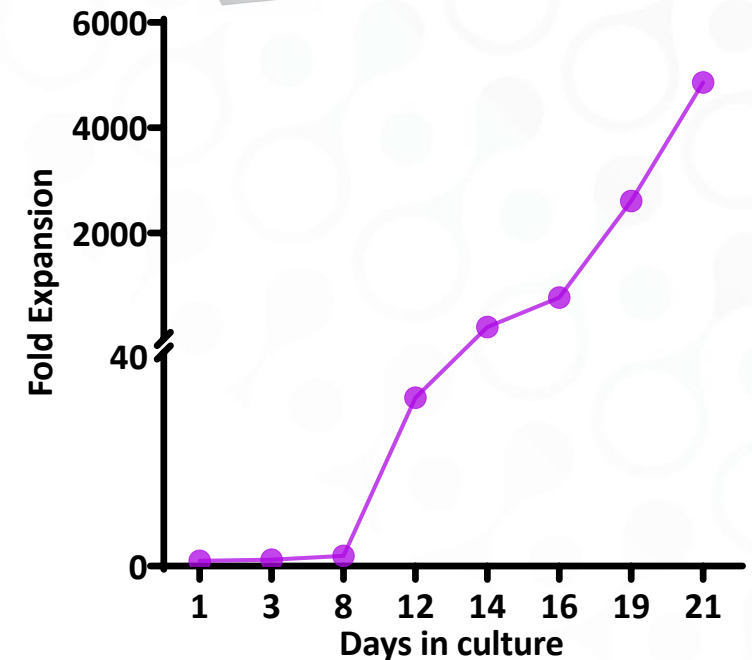
Expand to grow billions of CAR-iNKT cells



Vial and freeze CAR-iNKT cells



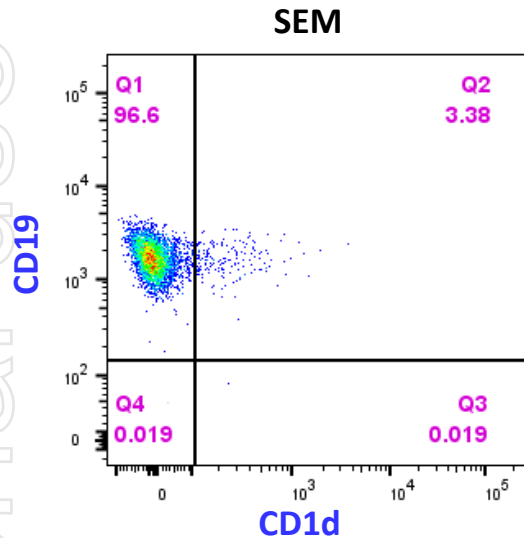
- iNKT cells from a healthy donor were modified to produce a CD19-targeting CAR using a 3<sup>rd</sup> generation lentiviral vector from Lentigen Technologies, Inc.
- Cells could be 'expanded' (multiplied) ~5,000-fold to produce large numbers of cells from a single batch
  - Expansion is key to producing an off-the-shelf therapy that addresses the logistical challenges of current autologous cell therapies and provides higher commercial returns through lower manufacturing costs



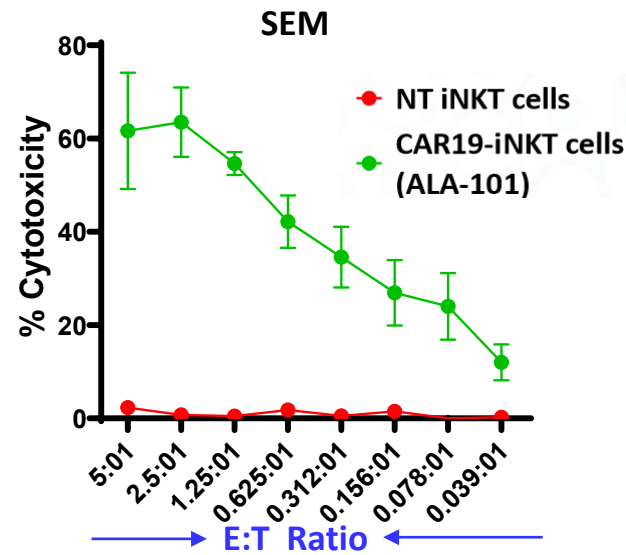
AACR Poster Fig 2(D)

# ALA-101 Kills Tumour Cells That Express CD19

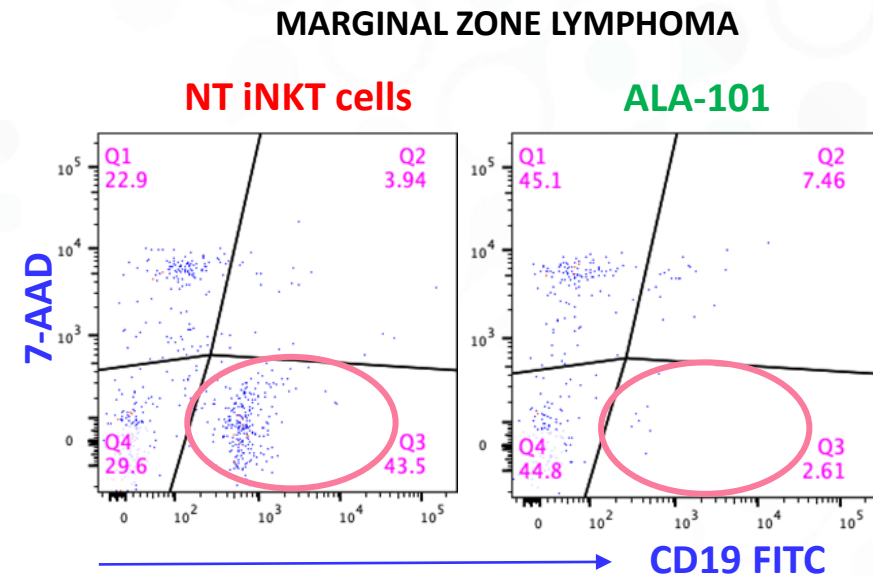
- SEM cells originate from a patient with an aggressive form of B-cell Acute Lymphoblastic Leukemia and express CD19, but not CD1d.
- ALA-101 cells efficiently kill multiple leukemia cells lines, including SEM
- ALA-101 eradicated >90% of viable CD19+ cells from a marginal-zone lymphoma patient sample



AACR Poster Fig 3(A)



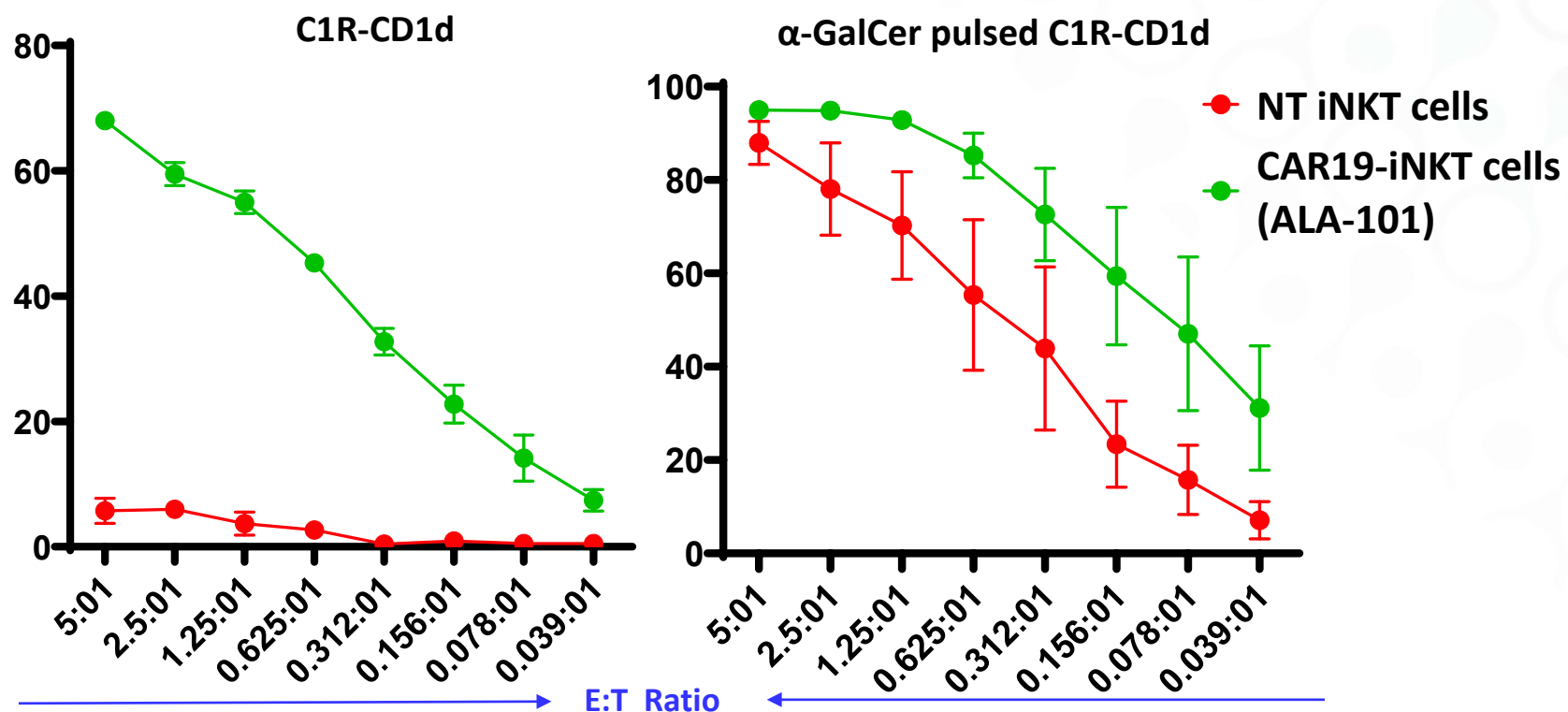
AACR Poster Fig 3(C)



AACR Poster Fig 3(B)

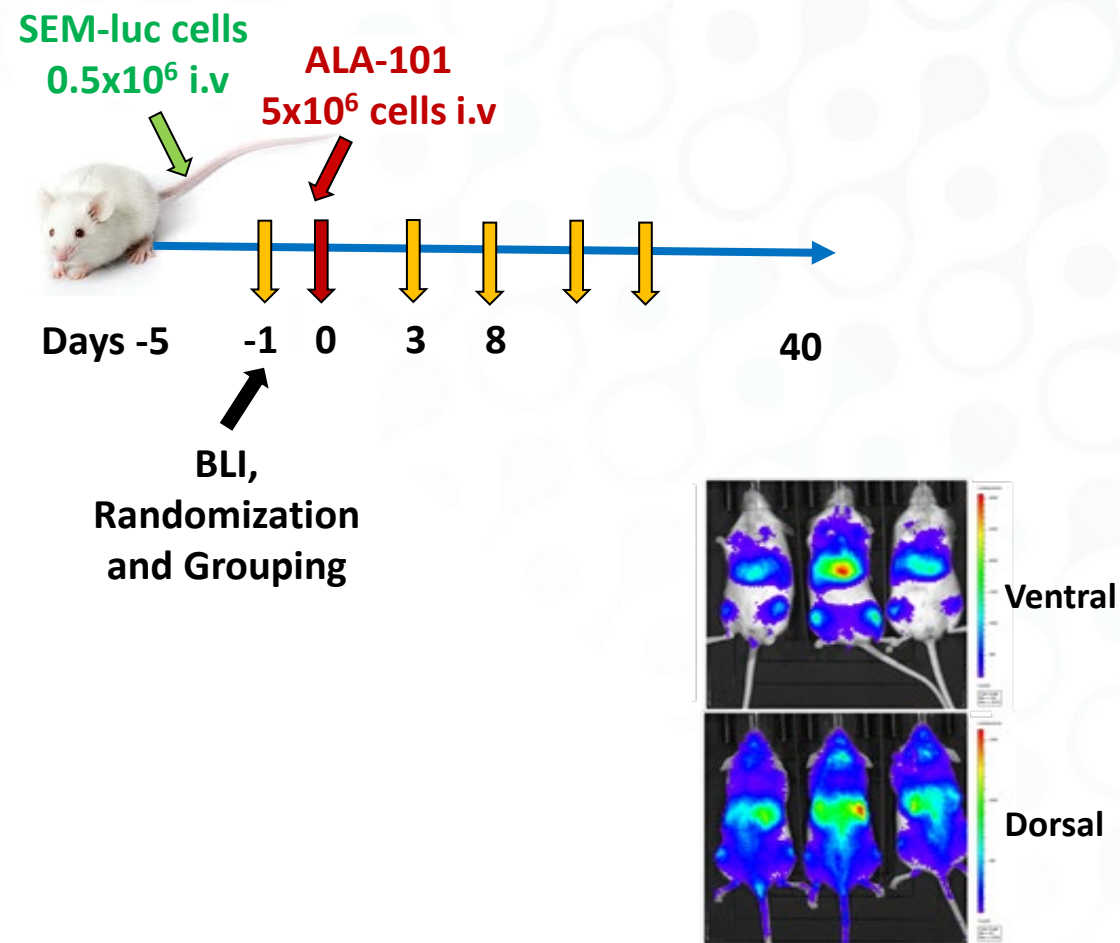
# ALA-101 is Dual Targeting

- 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  $\alpha$ -GalCer



# ALA-101 is Effective in an Aggressive Leukemia Model

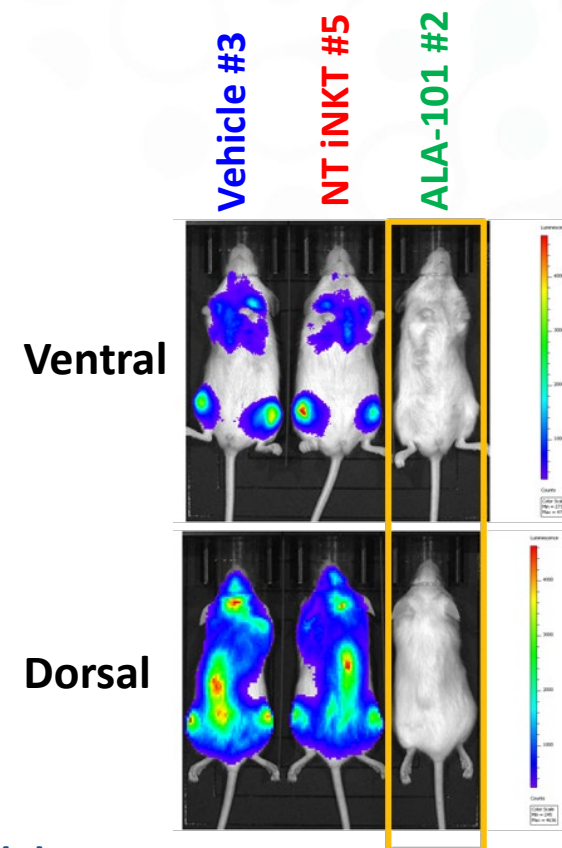
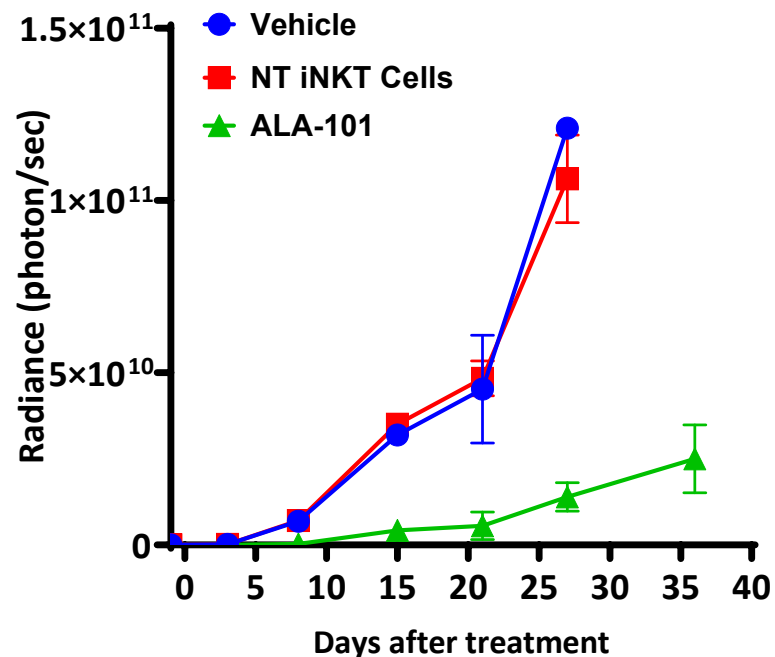
- ALA-101 was tested in mouse model of B-Cell Acute Lymphoblastic Leukemia (B-ALL) model
- Mice were transplanted with SEM cells originating from a patient with an aggressive form of B-ALL
- After the tumour was established, mice were treated with a relatively low dose of ALA-101



Bioluminescence showing tumour engraftment at Day -1

# ALA-101 Dramatically Reduced Tumour Burden

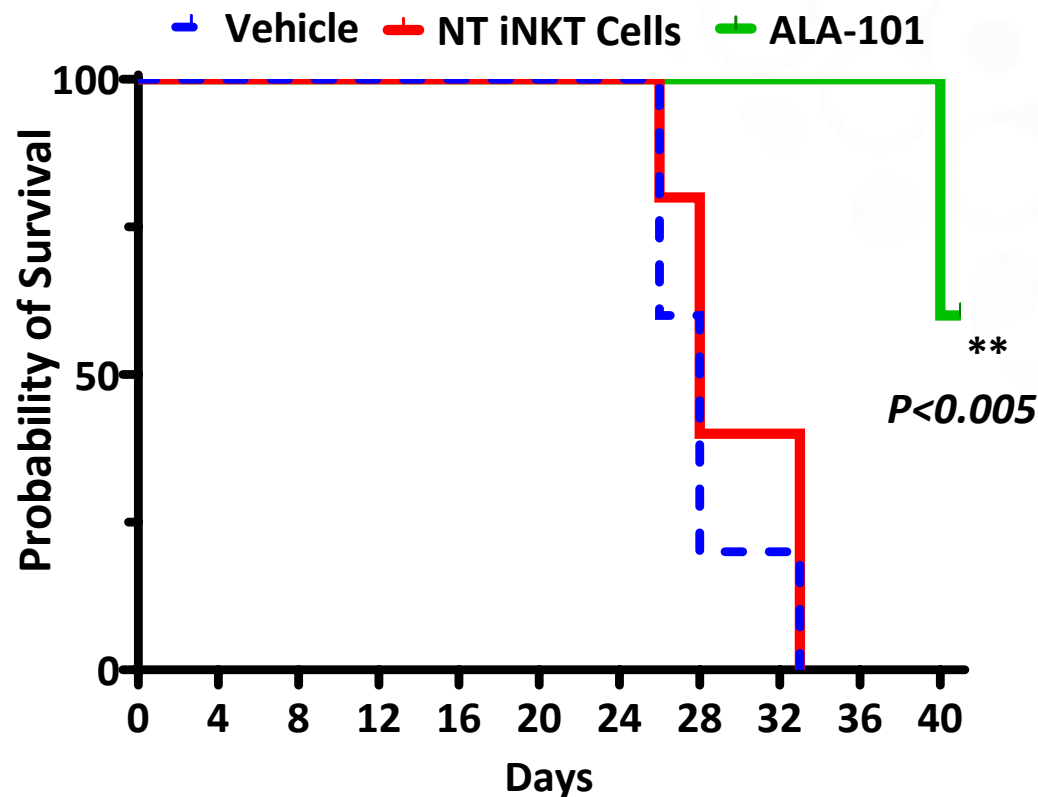
- After 26 days, tumour burden in ALA-101-treated mice was ~90% lower than control animals
- Bioluminescent imaging reveals substantially lower tumour burden in ALA-101-treated animals on Day 8



AACR Poster Fig 5(B) & (E)

# ALA-101 Significantly Increased Animal Survival

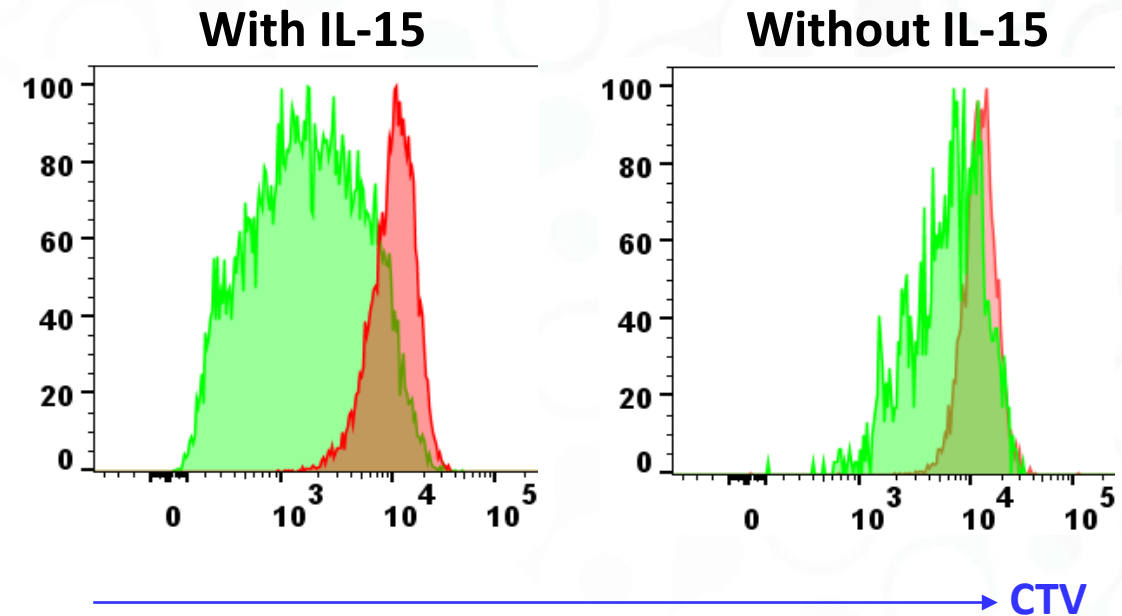
- ALA-101 significantly enhanced the survival of the mice over untreated controls ( $p < 0.005$ )



AACR Poster Fig 5(C)

# Expanded iNKT Cells Retain the Ability to Proliferate

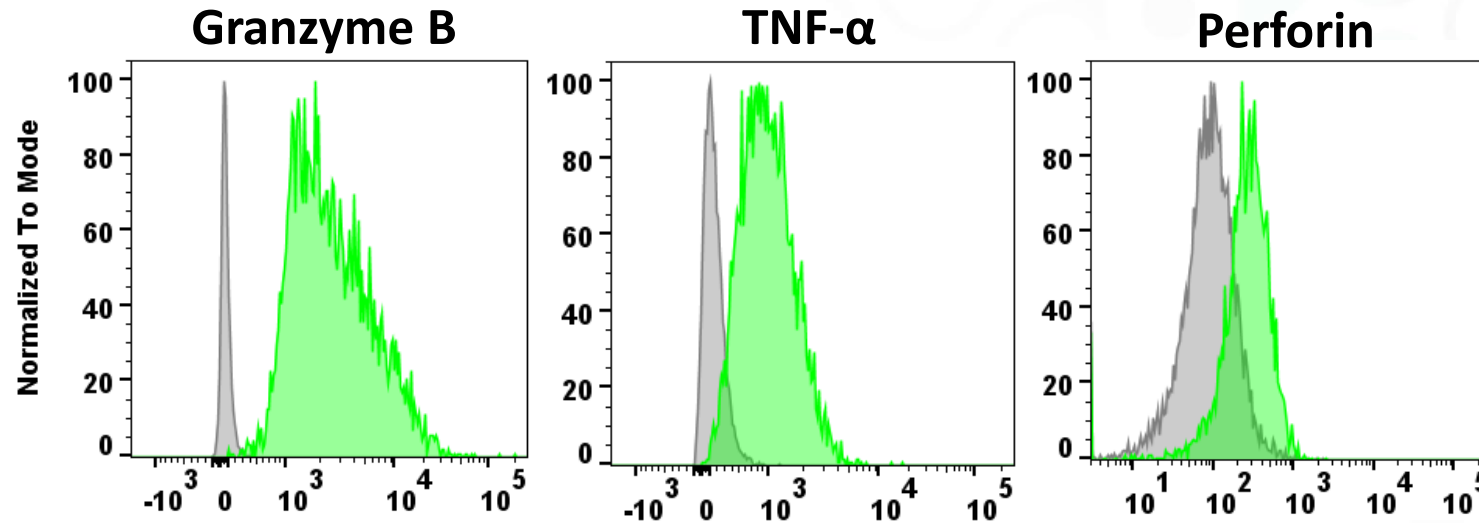
- ALA-101 cells that had been expanded ~5,000 fold were labeled with a fluorescent dye (CTV)
- Cells were then exposed to SEM tumour cells that were either **positive (CD19+)** or **negative (CD19-)** for CD19 expression on their surface
- Upon exposure to **CD19+** tumour cells, ALA-101 cells continued 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**



AACR Poster Fig 4(B)

# 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- $\alpha$  and Perforin



AACR Poster Fig 4(A)

# 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



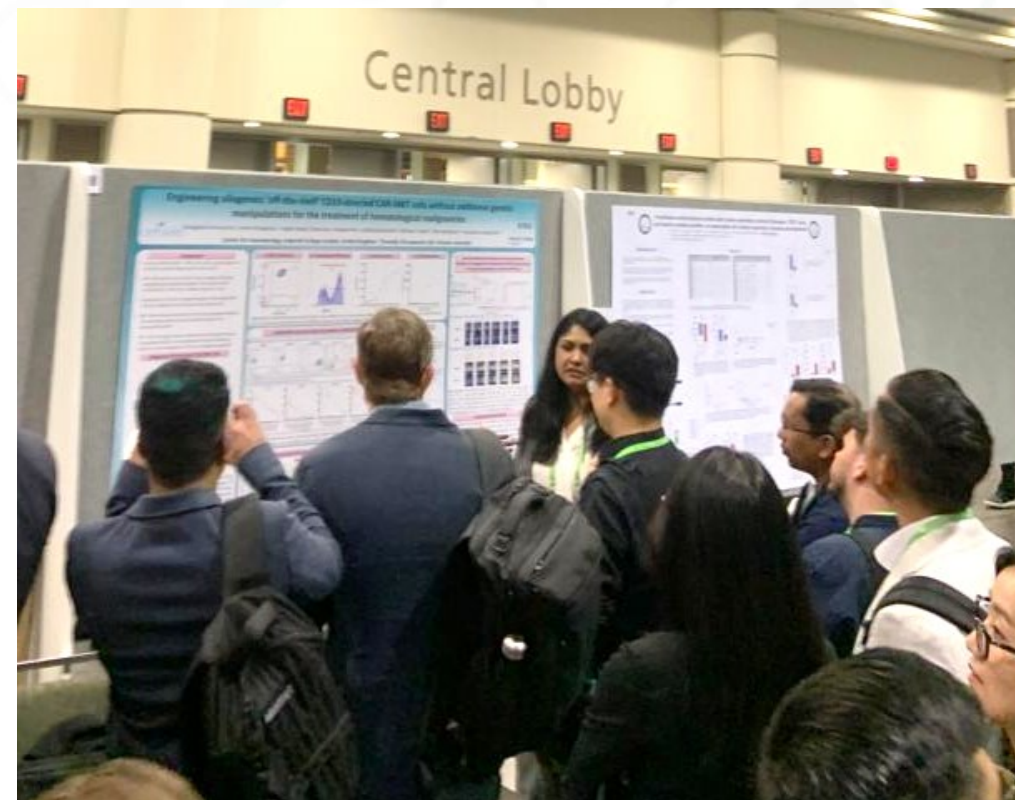
- ALA-101 conferred significant anti-tumour effect and significantly extended lifespan in an aggressive model of human B-Cell Acute Lymphoblastic Leukemia (B-ALL)
  - Confirming the potential of ALA-101 as an effective treatment for CD19+ leukemias and lymphomas

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



aróvella  
THERAPEUTICS

1. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC743650/>
2. <https://pubmed.ncbi.nlm.nih.gov/30300581/>
3. <https://link.springer.com/article/10.1007/s00441-010-1023-3>
4. <https://pubmed.ncbi.nlm.nih.gov/23824629/>
5. <https://escholarship.org/uc/item/127714/12828/14747?x=number-of-leverant-natural-kills-1-0>



18

# ALA-101 Scale-Up and Preparation for Clinical Material



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



Identify high-frequency iNKT  
cell donors



Optimise manufacturing process to  
produce clinical-grade material

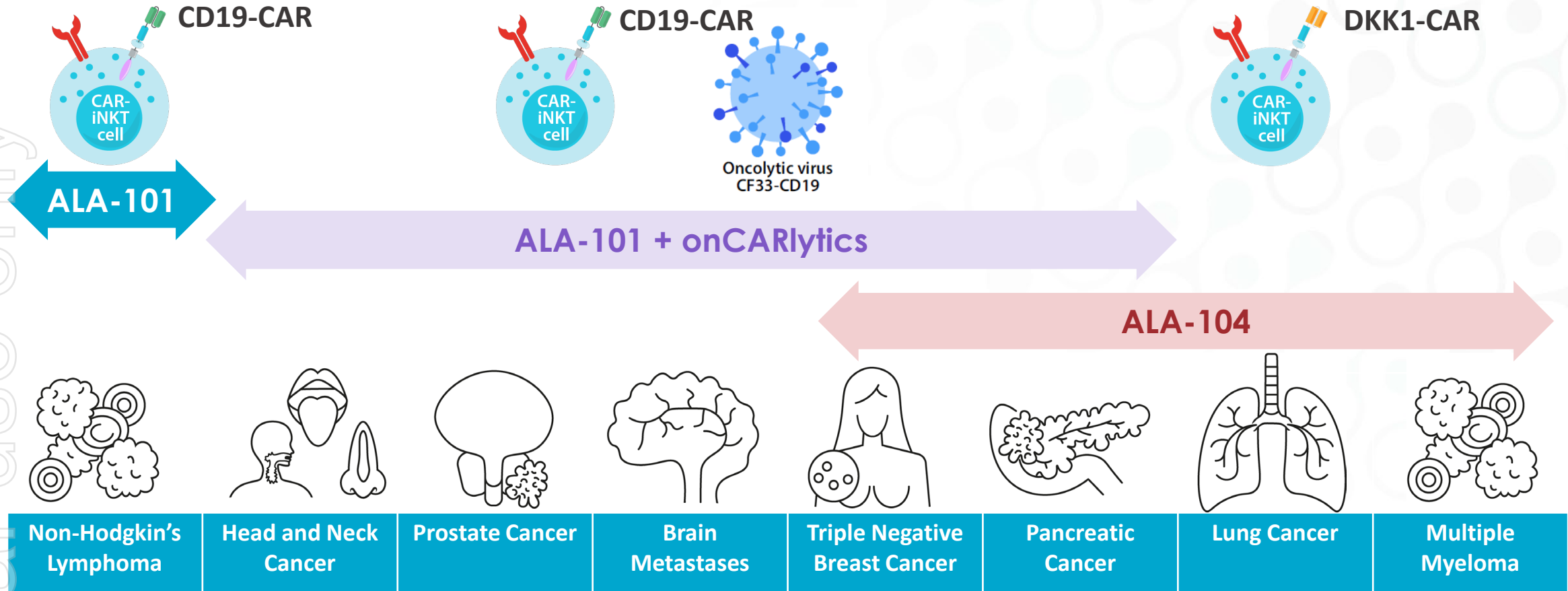


Scale-up and generate data required  
for regulatory submissions



Produce clinical  
material


# Arovella's Potential Cancer Targets



Additional CARs can be used to target different cancer types:

- Blood Cancers** - CD20, CD22, CD79b; **Solid tumours** – mesothelin, EGFRvIII, IL13 $\alpha$ 32, GPC3, HEPG2, GD2

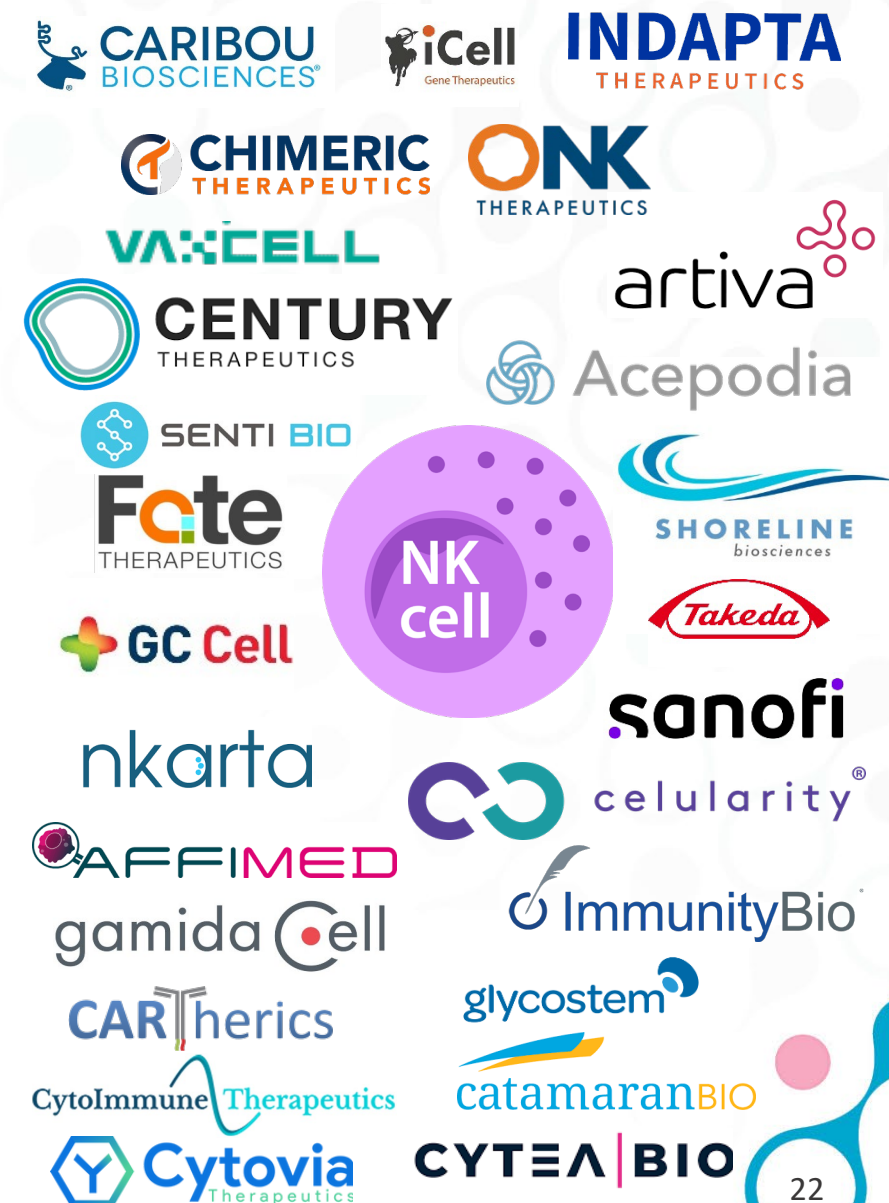
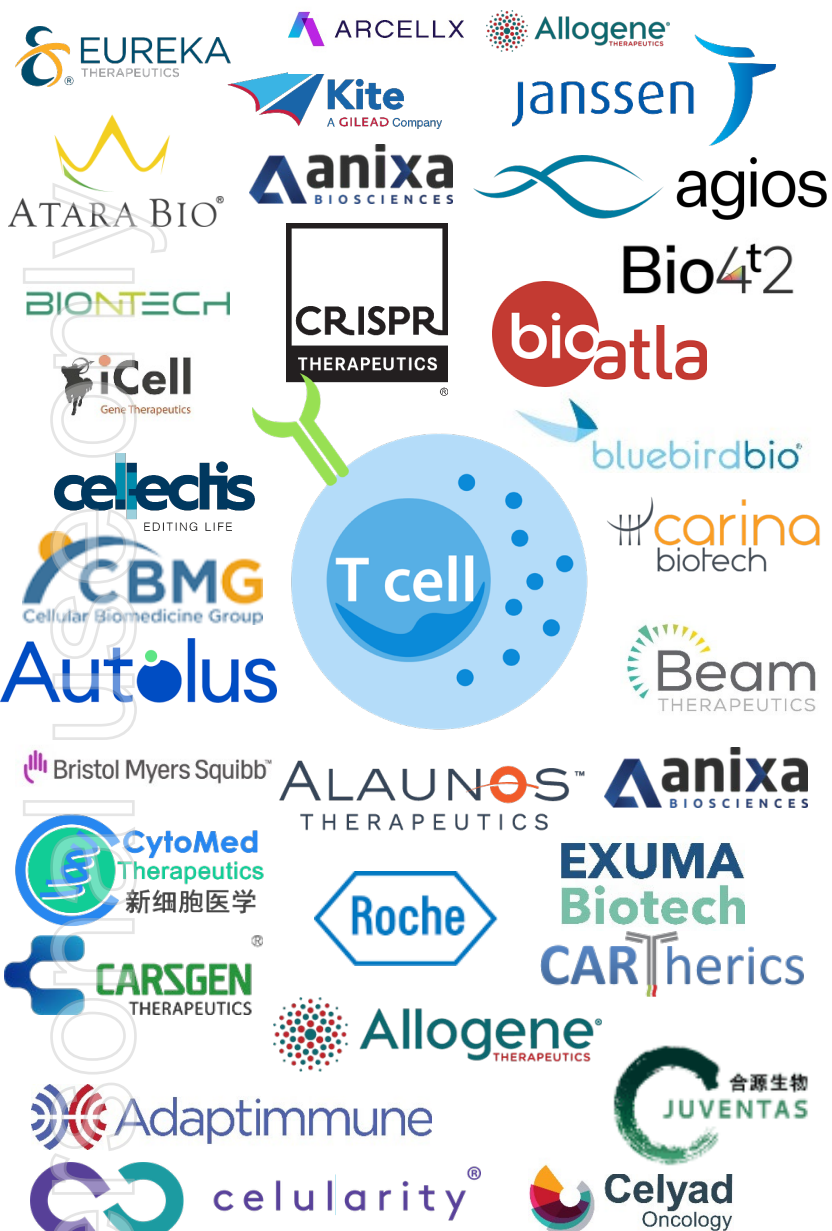
# Arovella's Key Milestones Over 18 Months

Cell Therapy							
	Partner	Discovery	Lead Optimisation	IND-Enabling	Phase 1		
CAR19-iNKT (ALA-101)		CD19 Expressing Lymphoma					
ALA-101 + onCARlytics		Solid Tumours					
		Multiple Myeloma					
DKK1-CAR-iNKT (ALA-104)		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

# The Potential of CAR-iNKT Cells is Untapped



# 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 <small>A Member of the Roche Group</small>	 ArsenalBio™	Preclinical	\$70	undisclosed	
Aug-22	Licence and strategic collaboration	 Roche	 POSEIDA THERAPEUTICS	Phase I	\$110	\$110	\$220
Sep-21	Development collaboration	 Genentech <small>A Member of the Roche Group</small>	 Adaptimmune	Preclinical	\$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
<b>Mean</b>					<b>\$134</b>	<b>\$208</b>	<b>\$364</b>

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

Source: Company analysis based on public information

# Arovella Financial Overview

## Financial Snapshot

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

## Major Shareholders

Shareholder	Ownership (%) <sup>1</sup>
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

### ALA Price and Volume - 12 Months<sup>1</sup>



# Arovella Has a Strong Leadership Team

## LEADERSHIP

# Imperial College London



Dr. Michael Baker  
**CEO & MANAGING DIRECTOR**



Dr. Nicole van der Weerden  
**CHIEF OPERATING OFFICER**



Dr. Mini Bharathan  
**SENIOR VP DEVELOPMENT & TRANSLATIONAL MEDICINE**



Dr. Robson Dossa  
**SENIOR DIRECTOR  
MANUFACTURING & QUALITY**



Ana Radeljevic  
**BUSINESS DEVELOPMENT**



## BOARD OF DIRECTORS



Dr. Tom Duthy  
**BOARD CHAIR**



Dr. Elizabeth Stoner  
**DIRECTOR**



Dr. Debora Barton  
**DIRECTOR**



Mr. Gary Phillips  
**DIRECTOR**



Mr. David Simmonds  
**DIRECTOR**



# Thank you

Want to hear more?  
Catch-up on our recent  
Explanatory Webinar online to  
hear the full ALA-101 story!

Email: [investor@arovella.com](mailto:investor@arovella.com)



ASX: ALA



## Explanatory Webinar

EVENT SPEAKERS



**Dr. Mini Bharathan**  
SENIOR VP DEVELOPMENT &  
TRANSLATIONAL MEDICINE



**Dr. Michael Baker**  
CEO & MANAGING  
DIRECTOR

**On-Demand Replay  
Available Now**

**Click to access or go to**  
<https://www.youtube.com/watch?v=NopK25X6YXI>