

**ASX: ALA**

Arovella Therapeutics Limited  
ACN 090 987 250



**ASX Release**

25 July 2023

**AROVELLA PRESENTS AT THE 17<sup>TH</sup> ANNUAL BIOSHARES BIOTECH SUMMIT**

**Highlights:**

- **Arovella presents its novel iNKT cell therapy platform at the 17<sup>th</sup> Annual Bioshares Biotech Summit in Hobart.**

**MELBOURNE, AUSTRALIA 25 July 2023:** Arovella Therapeutics Ltd (ASX: ALA), a biotechnology company focused on developing its invariant Natural Killer T (iNKT) cell platform to treat cancer, today presents at the 17<sup>th</sup> Annual Bioshares Biotech Summit in Hobart.

Arovella's CEO and MD, Dr Michael Baker, will present data describing the key benefits of Arovella's proprietary iNKT cell therapy platform as truly "off-the-shelf" with the potential for improved efficacy across a range of oncology indications.

Highlights from the presentation include:

- The "off-the-shelf" capabilities of Arovella's CAR-iNKT platform
- Potential benefits of CAR-iNKT cells over CAR-T in treating cancers
- Key advantages of Arovella's proprietary manufacturing process
- The history of iNKT cells as a novel cell type and CAR-iNKT cells as a new treatment opportunity
- The potential of ALA-101 in combination with Imugene's onCARlytics platform to treat solid tumours
- The possibility of Arovella's proprietary iNKT cell platform with novel CARs to target solid tumours

The presentation is attached to this announcement and can be viewed on the Company's website [www.arovella.com.au](http://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**

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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 (iTTCR) 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.

**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.

For more information, visit [www.arovella.com](http://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.

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T H E R A P E U T I C S

ASX:ALA

**17<sup>th</sup> Bioshares Biotech Summit**  
July 2023



**17TH BIOSHARES BIOTECH SUMMIT**

*The Essential Biotech Investment Event*

24-25 July 2023 Hobart Tasmania

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# Arovella Therapeutics Highlights



## Off-the-Shelf iNKT Cell Platform

Arovella is developing off-the-shelf iNKT cell therapies to target blood cancers and solid tumour cancers



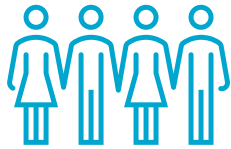
## Lead Product Advancing to Clinic

ALA-101, a potential treatment for CD19-expressing blood cancers, is being progressed to phase I clinical trials, expected to commence in 2024



## Addressing Key Unmet Need

Arovella's iNKT cell platform is well positioned to solve key challenges that hamper the cell therapy sector



## Strong Leadership Group

Arovella's leadership team and its Board have proven experience in drug development, particularly cell therapies



## Strategic Acquisitions

Arovella is 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

# Arovella Financial Overview

## Financial Snapshot

ASX CODE	ALA
Market capitalisation <sup>1</sup>	\$43.1 million
Shares on issue	899.1 million
52-week low / high <sup>1</sup>	\$0.020 / \$0.105
Pro Forma Cash (June 30 2023 + SPP) <sup>2</sup>	\$7.38 million

## Major Shareholders

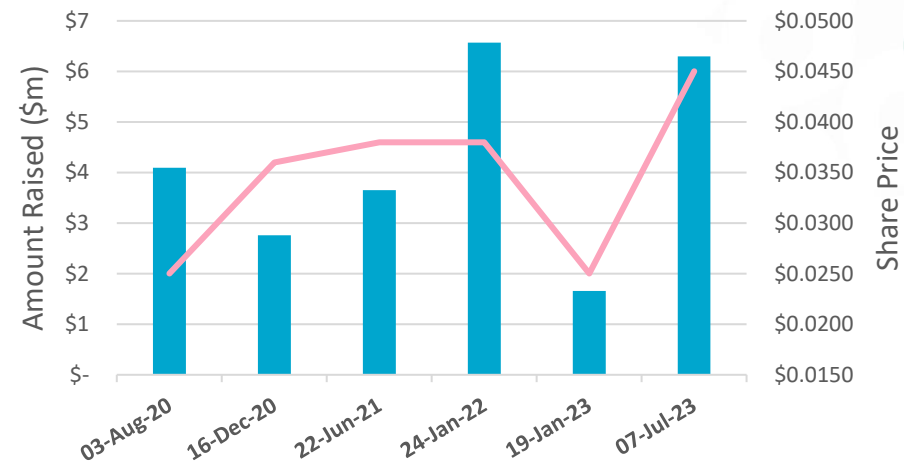
Shareholder	Ownership (%) <sup>1</sup>
MERCHANT FUNDS MANAGEMENT PTY LTD	86,210,282 (11.36%)
RICHARD JOHN MANN	54,458,288 (6.40%)
UBS NOMINEES PTY LTD	20,620,196 (2.45%)
BLACKBURNE CAPITAL PTY LTD	18,250,000 (2.17%)
DYLIDE PTY LTD	15,000,000 (1.78%)

1. As of 19 July 2023
2. Includes \$2.2m from the SPP that closed 6 July 2023, but not funds from the R&D tax incentive rebate expected before November 2023

## ALA Price and Volume - 12 Months



## ALA Capital Raise History



# What are “CAR-T Cells”?

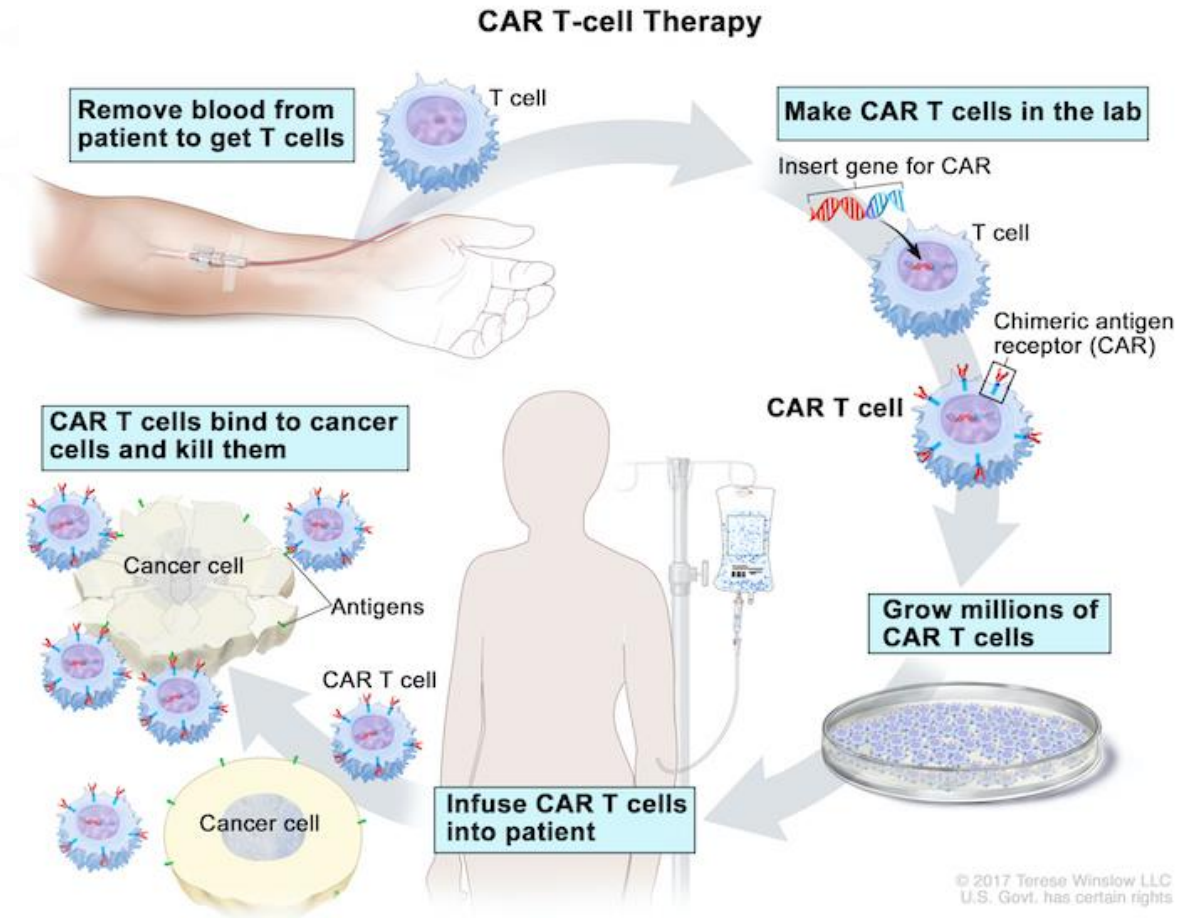
- T cells are a common type of immune cell that fight infections and can help fight cancer

- 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 specifically recognises cancer cells through a target antigen

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



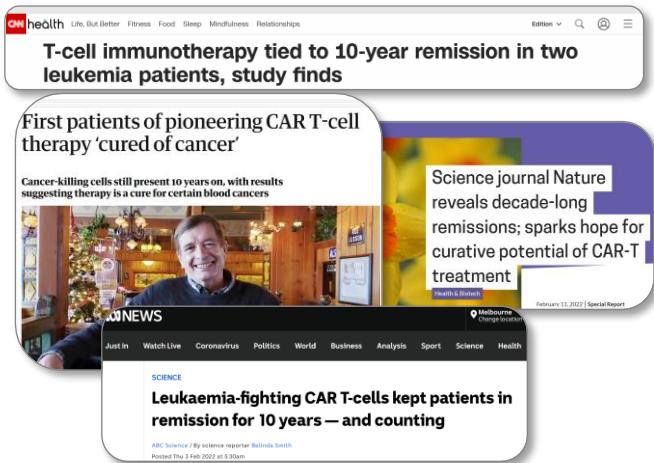
<https://www.ohsu.edu/sites/default/files/2021-04/CAR%20TcellTherapy7-700px.jpg>

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# Cell Therapy Has Revolutionized Blood Cancer Treatment

- CAR-T cells have demonstrated ability to **cure** haematological cancers and have generated strong sales
- The Cell Therapy market is expected to reach \$61.2 billion by 2030<sup>1</sup>

## February 2022



## May 2022



Product	Approval Year	2022 Revenue
 YESCARTA <sup>®</sup> (axicabtagene ciloleucel) <small>Suspension for IV infusion</small>	2017	US\$1160m <sup>2</sup>
 KYMRIAH <sup>®</sup> (tisagenlecleucel) <small>Suspension for IV infusion</small>	2017	US\$536m <sup>3</sup>
 Abecma <sup>®</sup> (idecabtagene vicleucel) <small>Suspension for IV infusion</small>	2021	US\$388m <sup>4</sup>

1. <https://www.businesswire.com/news/home/20230529005130/en/Global-Cell-Therapy-Market-Report-2023-Advancements-in-Biotechnology-Drives-Growth---ResearchAndMarkets.com>
2. [https://s29.q4cdn.com/585078350/files/doc\\_financials/2022/q4/GILD-Q4-FY22-Earnings-Press-Release-2-February-2023.pdf](https://s29.q4cdn.com/585078350/files/doc_financials/2022/q4/GILD-Q4-FY22-Earnings-Press-Release-2-February-2023.pdf)
3. [https://www.novartis.com/sites/novartis\\_com/files/q4-2022-media-release-en.pdf](https://www.novartis.com/sites/novartis_com/files/q4-2022-media-release-en.pdf)
4. <https://bioprocessintl.com/bioprocess-insider/therapeutic-class/bms-sees-car-t-sales-rocket-in-line-with-increased-capacity/#:~:text=For%20the%20full%20year%202022,%2487%20million%20the%20year%20prior.>



# But...Manufacturing and Logistics Pose Major Challenges

- **T cells must originate from the patient to be treated** so each manufacturing batch is patient-specific
  - **High manufacturing and supply chain costs** lead to high drug costs (>\$500k per patient)
  - Starting material (T cells) can be compromised due to disease, **reducing efficacy**
  - Limited number of centres able to collect cells and manufacture the therapy so **not all eligible patients can be treated**

## Manufacturing CAR-T takes 4-6 weeks for each patient

- Patients with aggressive disease sometimes **die while waiting for treatment**
- **Manufacturing run failures can occur**, further increasing the time to treatment (and cost)

Arovella's allogeneic CAR-iNKT cell platform has the potential to address the manufacturing and logistics challenges of CAR-T cells and the potential for improved efficacy



Autologous CAR-T 4-6 weeks

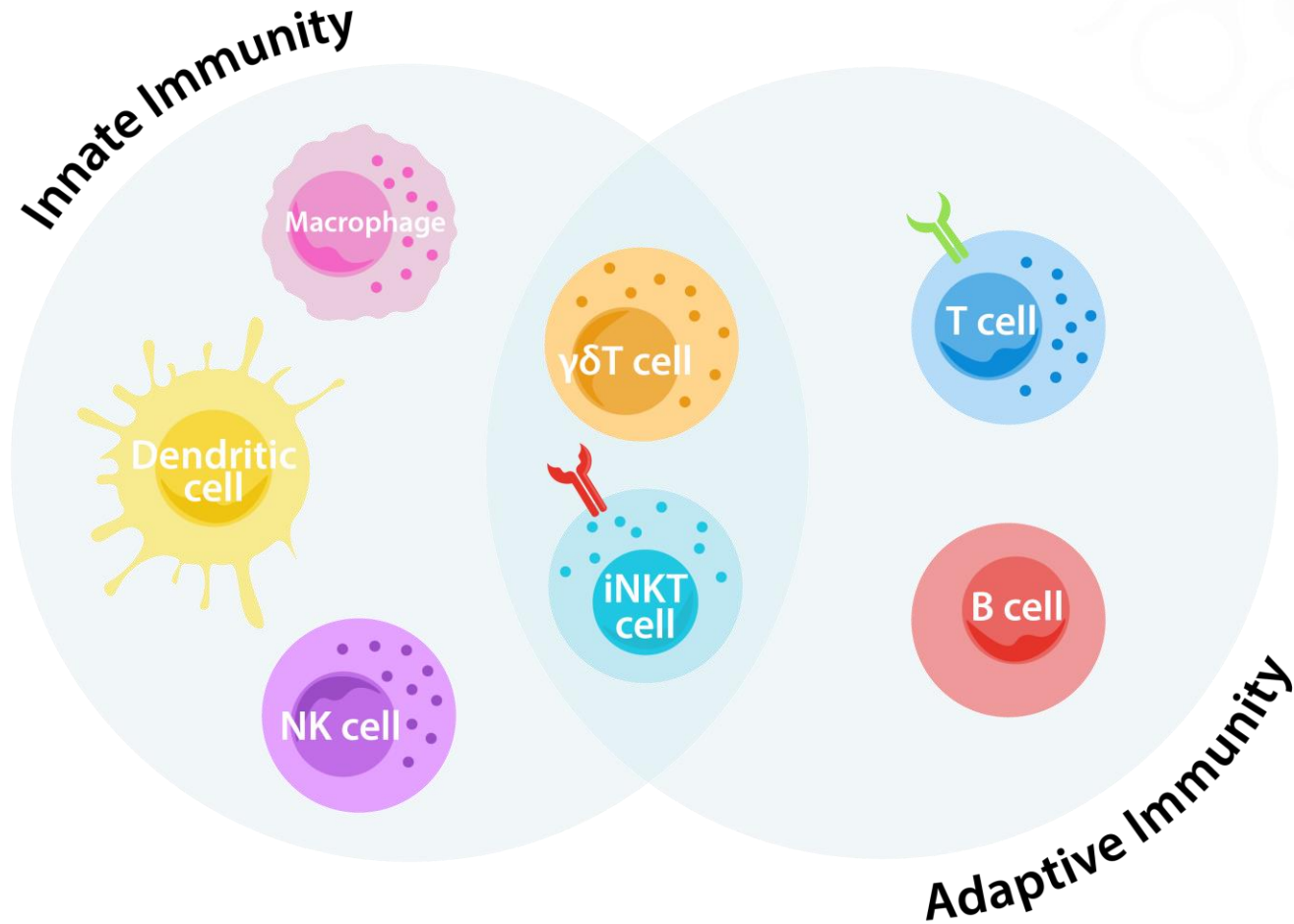


Allogeneic CAR-iNKT ~1 week



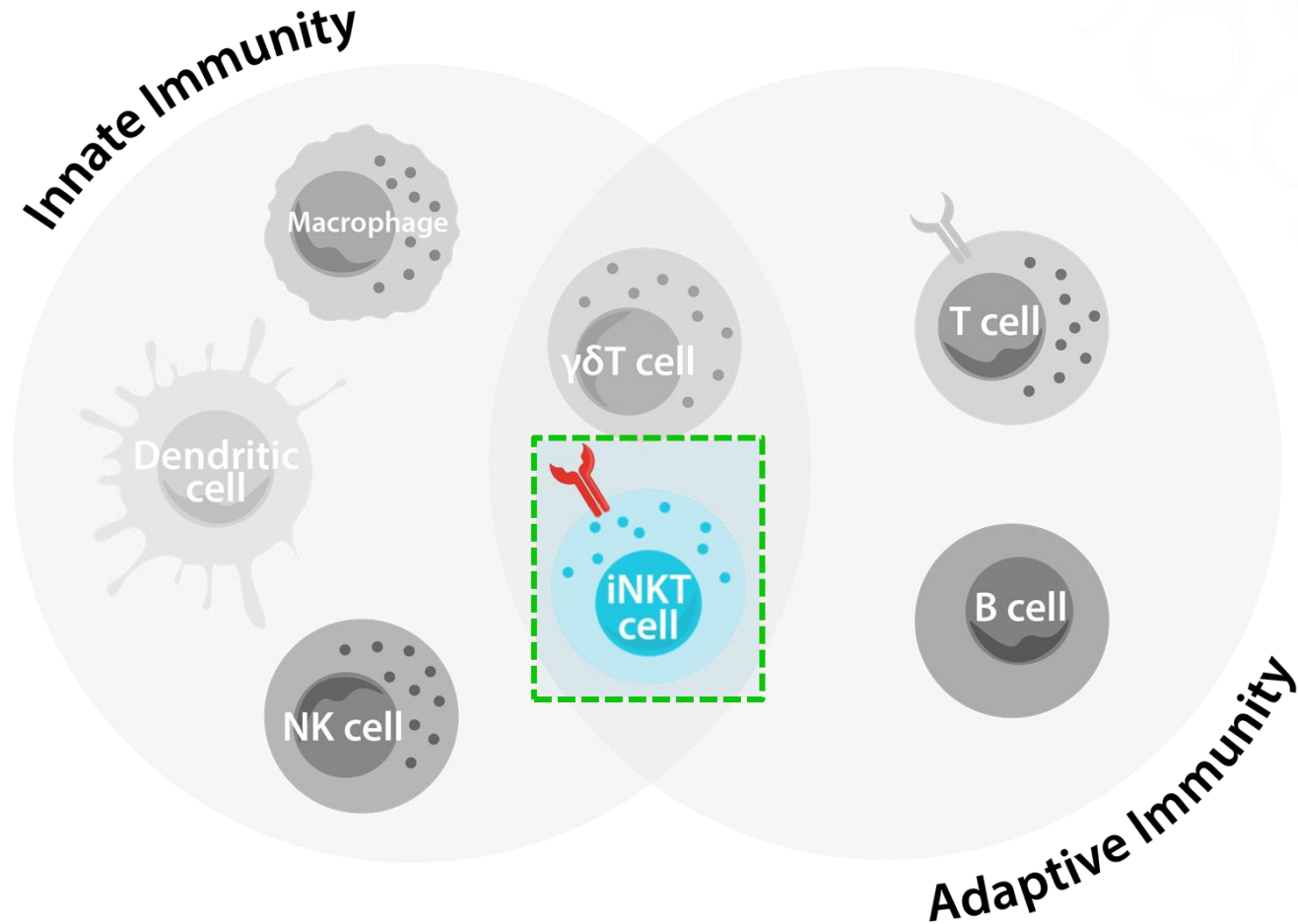
# Introducing invariant Natural Killer (iNKT) Cells

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# Introducing iNKT Cells

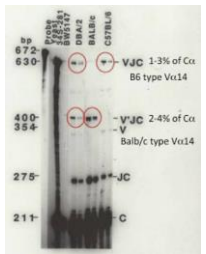
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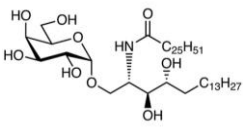
- Front line of the human immune system
- Bridge innate and adaptive immune responses
- Contain both T cell and NK cell killing mechanisms
- They do not cause graft versus host disease (GVHD)
- Naturally target and kill cancers that express CD1d
- Shape the tumour microenvironment by blocking/killing pro tumour cells (TAMs/MDSCs)
- Infiltrate tumours and secrete signaling molecules to activate other immune cells to kill tumour cells

# iNKT Cell Discovery and Therapeutic Evolution

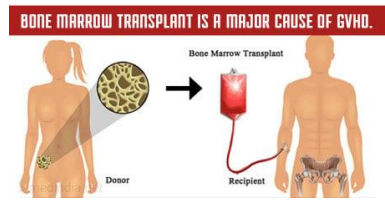
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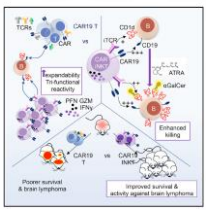
Murine iNKT cell discovery 1986



MHC Class I-like CD1d ligand discovered – αGalCer 1997



iNKT cells demonstrated to be protective against GVHD in humans 2012



Arovela's iNKT cell platform published in Cancer Cell 2018



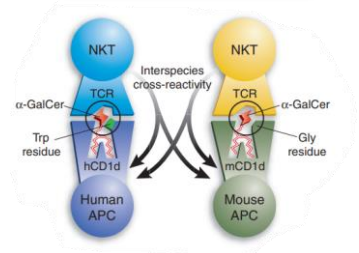
Appia exited stealth mode, raised \$52m and entered into an \$875m partnership with Kite Pharma 2021



Arovela licensed iNKT cell platform from ICL 2021

## Timeline

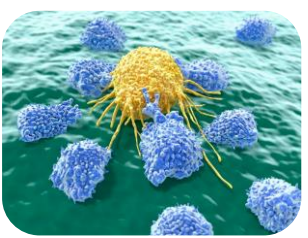
MHC Class I-like CD1d discovered 1997



First clinical trial stimulating iNKT cells *in vivo* was performed in patients with solid tumours 2002



First publication for CAR-iNKT cells 2014



First clinical trial data published for CAR-iNKT cells targeting neuroblastoma 2020



Kuur acquired by Athenex for \$185m 2021



MiNK IPO on the Nasdaq 2021



- T cell cytotoxicity studied in 1960s
- First CAR-T experiments 1985

# 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

# Why Are There Few iNKT Cell Players?

- Less well studied immune cell type
  - Requires expertise for culturing and experimentation
- Groups already working with T cells, NK cells or other immune cell types

iNKT cell frequency is low in peripheral blood

- CD4+ T cells – 25-60% of peripheral blood mononuclear cells (PBMCs)<sup>1</sup>
- CD8+ T cells – 5-30% of PBMCs<sup>1</sup>
- NK Cells – 5-20% of PBMCs<sup>2</sup>
- iNKT cells – 0.01%-1.18% of PBMCs<sup>3</sup>

For an autologous product targeting hematological malignancies, patients likely to have further reduced iNKT cell numbers

- Difficulties manufacturing

The intellectual property licensed from Imperial revolves around methods of manufacturing high numbers of highly potent CAR-iNKT cells

Arovella has made significant progress optimising the manufacturing process for clinical trials

1. Becker et al 2016 *Cancer Immunol Immunother* [10.1007/s00262-016-1792-y](https://doi.org/10.1007/s00262-016-1792-y)
2. <https://www.miltenyibiotec.com/AU-en/resources/macs-handbook/human-cells-and-organs/human-cell-sources/blood-human.html>
3. Bernin et al 2016 *Med Microbiol Immunol* [10.1007/s00430-016-0449-y](https://doi.org/10.1007/s00430-016-0449-y)

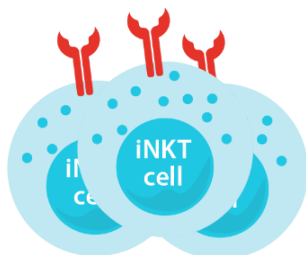
# CAR-iNKT Cell Therapy Production Advantages

## MANUFACTURING

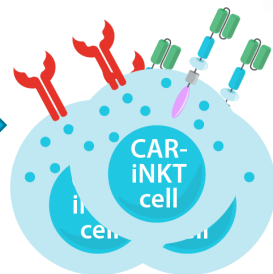
Collect Healthy Donor Blood



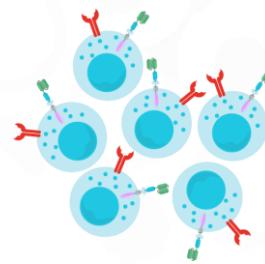
Isolate iNKT cells



Engineer iNKT cells to produce a CAR (i.e. ALA-101)



Expand to grow billions of CAR-iNKT cells



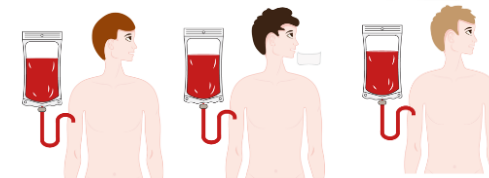
Vial and freeze CAR-iNKT cells



Thaw CAR-iNKT cells



Dose eligible patients



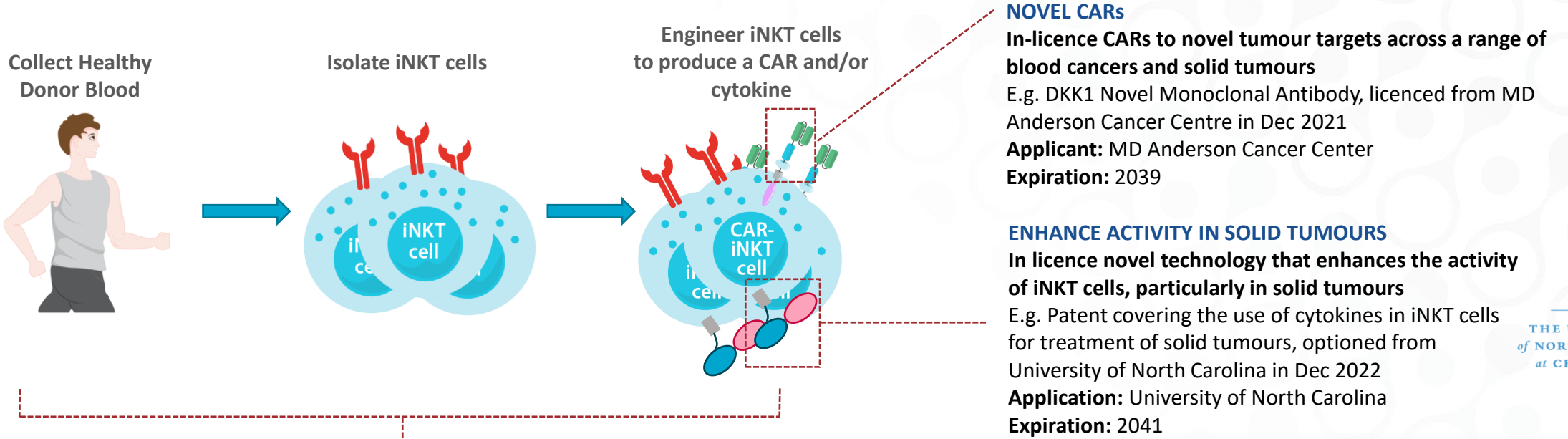
TREATMENT

## 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 Partnering Strategy In-licensing

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**Imperial College London**

## In-licensing Strategy

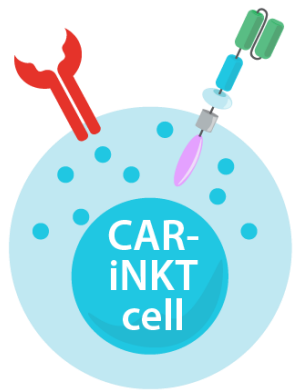
- Acquire intellectual property that enhances the iNKT cell platform and differentiates Arovella from competitors – CARs, cytokines, etc
- Determine the optimal arrangement based on the technology available – i.e. License or Option Agreement
- Consider Sponsored Research Agreements and SAB appointments





# Arovella's Partnering Strategy Co-Development

- ALA-101 contains a CAR targeting CD19 and is rapidly activated to kill CD19 expressing cancers<sup>1</sup>
- The product is being developed as an off-the-shelf product for cancer treatment



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THERAPEUTICS

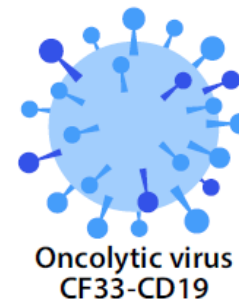
Imperial College  
London

Expecting *in vivo* data in  
H2 2023

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THERAPEUTICS

- <https://pubmed.ncbi.nlm.nih.gov/30300581/>
- <https://pubmed.ncbi.nlm.nih.gov/32032721/>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9126033/>

- CF33 is an oncolytic virus that targets tumour cells<sup>2</sup>
- CF33 has been engineered to induce CD19 expression after tumour cells have been infected – onCARlytics<sup>3</sup>
- Phase 1 trials for CF33 commenced October 2021 with CHECKvacc and May 2022 with VAXINIA
- FDA cleared IND for onCARlytics and Blincyto combination study in May 2023

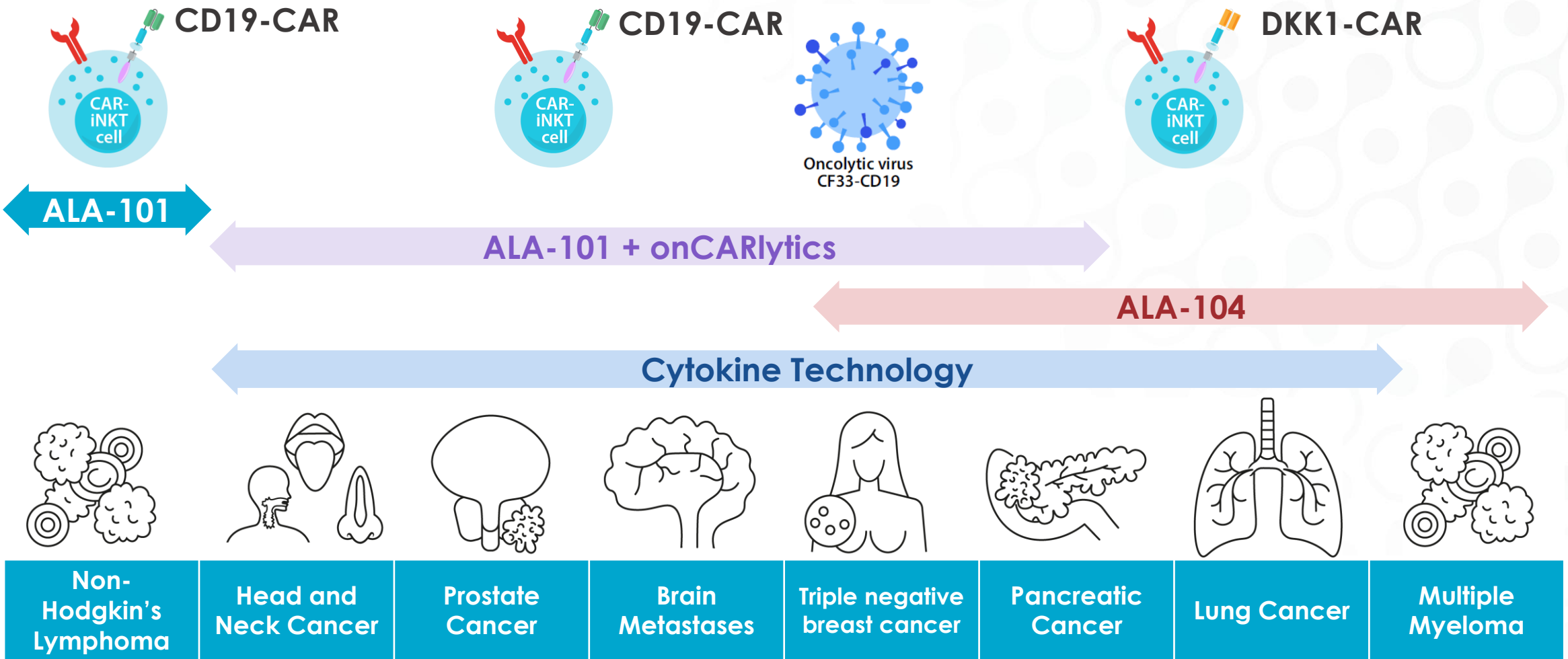


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Developing Cancer Immunotherapies

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# Arovella's Potential Cancer Targets

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

# ALA-101: Superior Activity Over CAR-T Cells

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

Tumour cells expressing CD19 and CD1d were intravenously delivered into mice

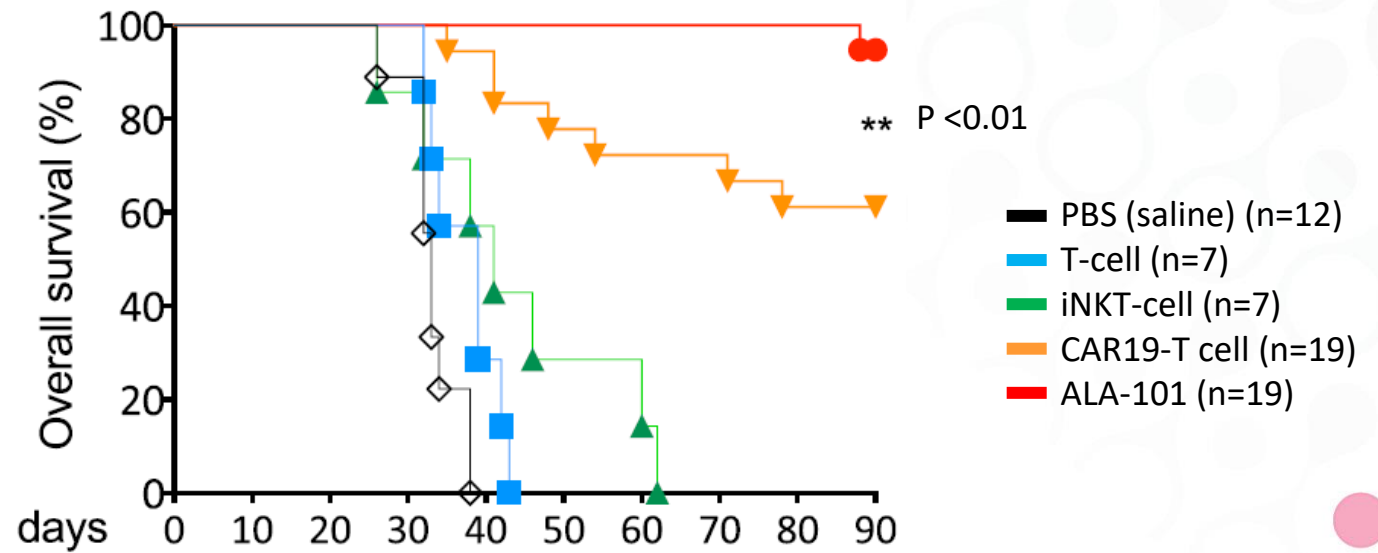
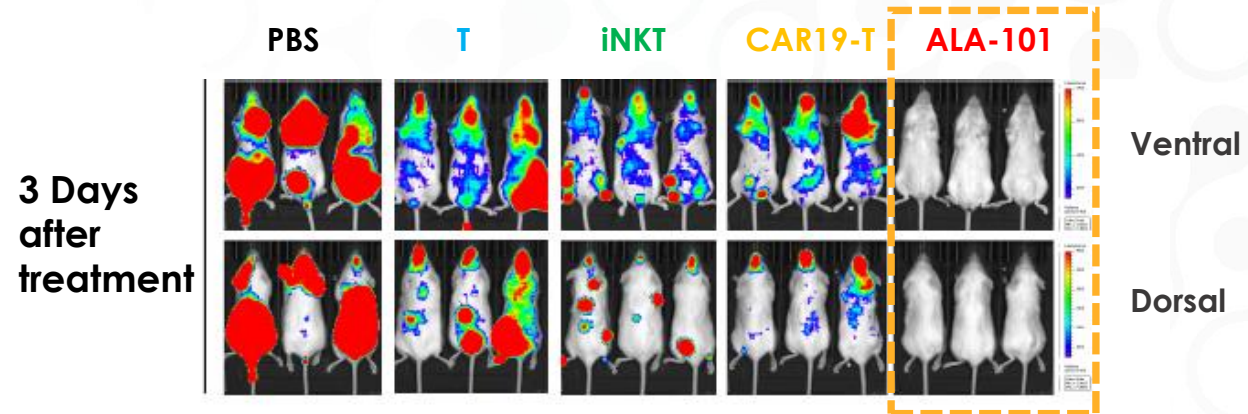
Mice were treated with:

- PBS (saline)
- Unmodified T cells (T)
- Unmodified iNKT cells (iNKT)
- CAR19-T cells
- ALA-101

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-expressing cancers**

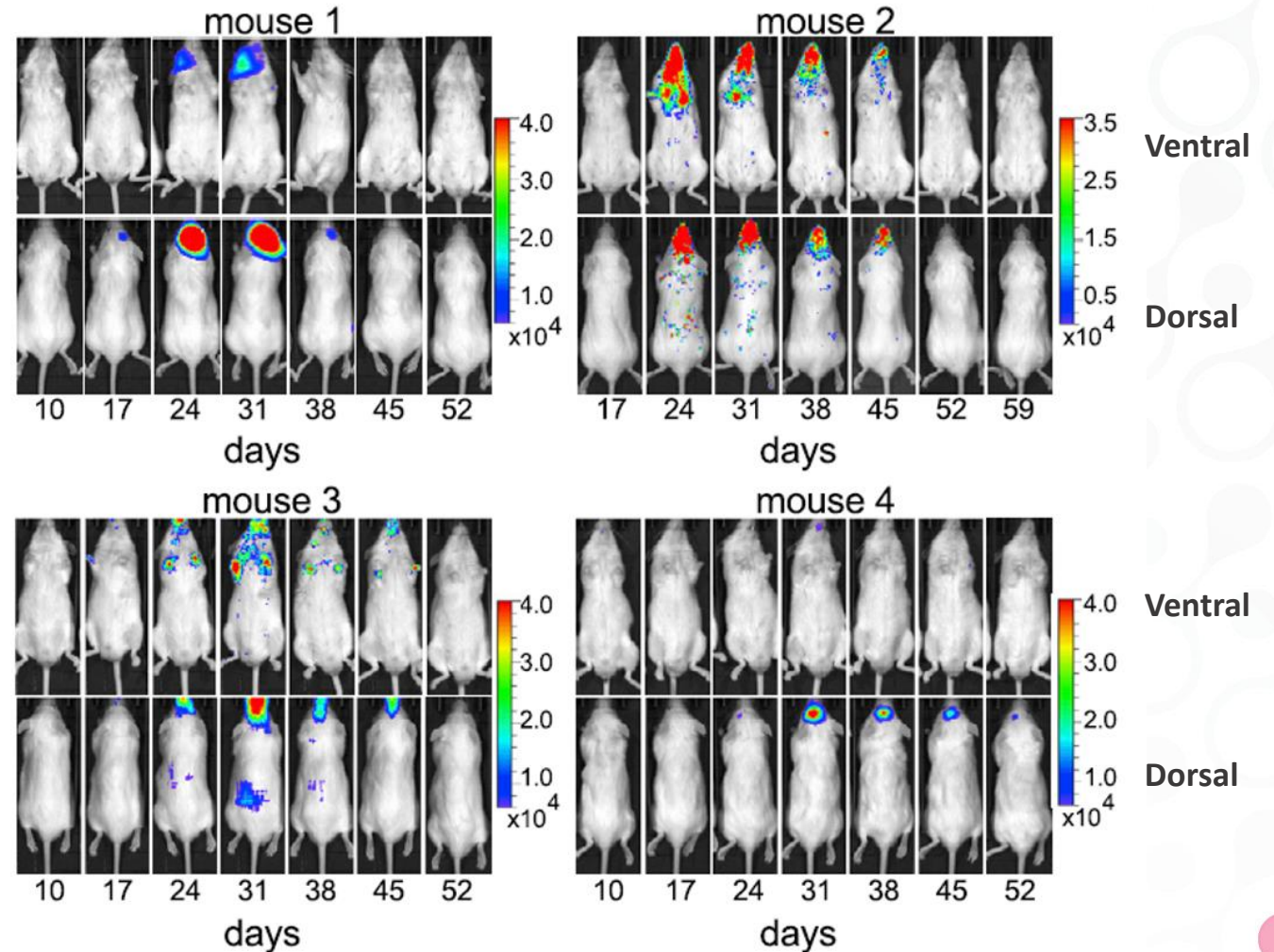


Rotolo et al., Cancer Cell (2018)

# 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 ALA-101 (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)

# Milestones FY2024

- Arovella expects to advance ALA-101 into a phase I first-in-human clinical trial during 2024
  - Non-Hodgkin’s lymphoma patients, dose escalation, primary end point – DLTs, secondary endpoint – efficacy signals
- Arovella also continues to assess novel complimentary technologies to expand the use of the iNKT platform to treat solid tumours

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June 2023

December 2023

June 2024

ALA-101




iNKT Cell Therapy Platform

- Complete process optimisation and scale-up in preparation for cGMP manufacture
  - Complete production of cGMP lentiviral vector
  - Finalise clinical trial plan for phase I study
- 
- Confirm the activity of CAR19-iNKT cells when combined with Imugene’s onCARlytics to target solid tumours in animal model
  - Analyse additional CARs to add to the platform
  - In-licence cytokine technology currently under option (pending positive data)

- Complete cGMP manufacture for phase I clinical trials
  - Complete preparatory activities for phase I study, including submission of regulatory dossier.
- 
- Initiate proof-of-concept testing for novel CARs and/or cytokine technology to expand iNKT platform for treatment of solid tumours

# Recent Cell Therapy Transactions

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Date	Type of deal	Acquirer/Licensee	Target/Licensor	Stage	Upfront (US\$M)	Milestones (US\$M)	Total deal value (US\$M)
May-23	License			Phase Ib	\$245	undisclosed	
Jan-23	Acquisition			Phase I	\$200	\$120	\$320
Oct-22	Development collaboration			Phase II	\$225*	undisclosed	
Sep-22	Research collaboration			Preclinical	\$70	undisclosed	
Aug-22	Licence and strategic collaboration			Phase I	\$110	\$110	\$220
Sep-21	Development collaboration			Preclinical	\$150	\$150	\$300
Aug-21	Research collaboration			Preclinical	undisclosed	undisclosed	\$875
May-21	Acquisition			Phase I	\$70	\$115	\$185
Jun-21	Acquisition			Preclinical	\$125	\$0	\$125
Dec-19	Acquisition			Preclinical	\$120	\$545	\$665
<b>Mean</b>					<b>\$146</b>	<b>\$208</b>	<b>\$364</b>

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

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# Thank You

**Dr. Michael Baker**  
CEO & Managing Director

Email: [investor@arovella.com](mailto:investor@arovella.com)  
Mobile: +61 403 468 187

