ASX Release

25 July 2023

AROVELLA PRESENTS AT THE 17TH ANNUAL BIOSHARES BIOTECH SUMMIT

Highlights:

- **Arovella presents its novel iNKT cell therapy platform at the 17th 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 17th 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.

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 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.

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.

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.

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ASX:ALA

17th 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

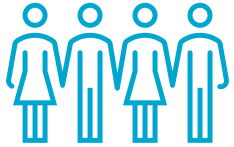
Arovella is developing off-the-shelf iNKT cell therapies to target blood cancers and solid tumour cancers

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

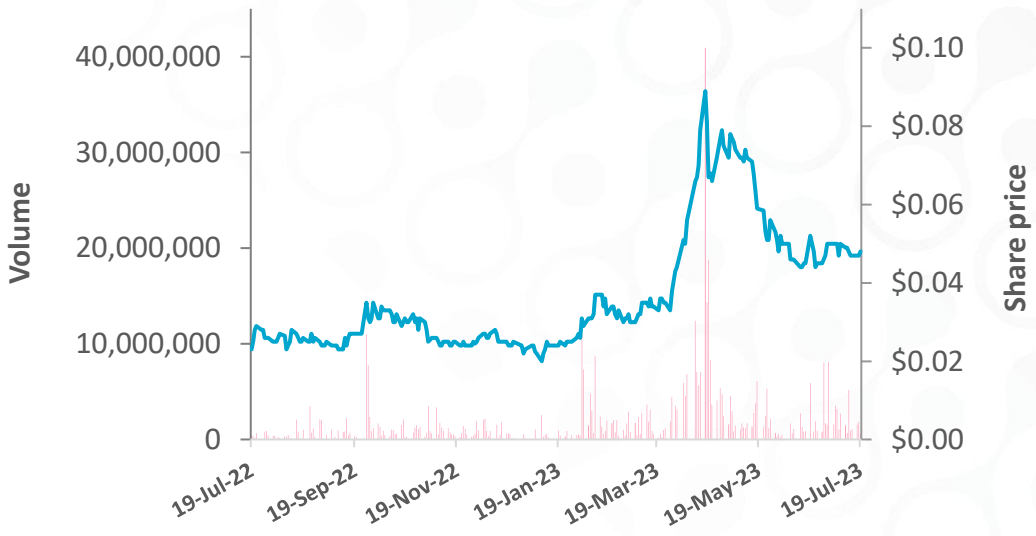
Financial Snapshot

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

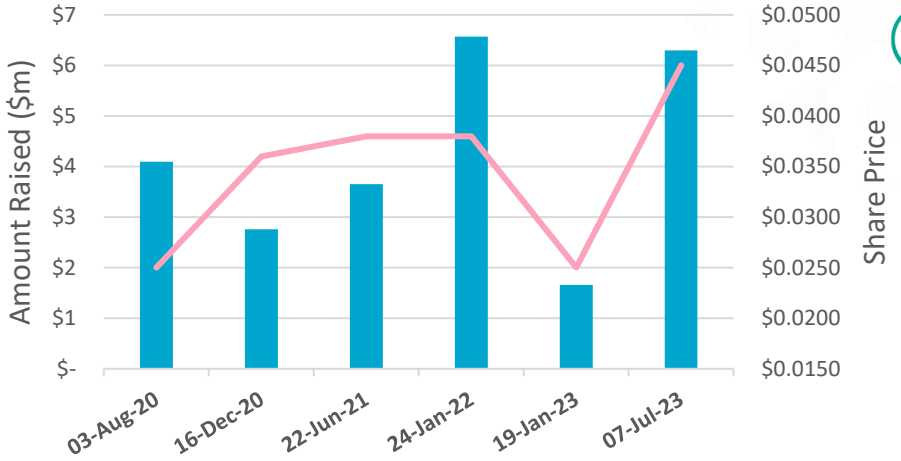
Major Shareholders

Shareholder	Ownership (%)[1]
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%)

ALA Price and Volume - 12 Months



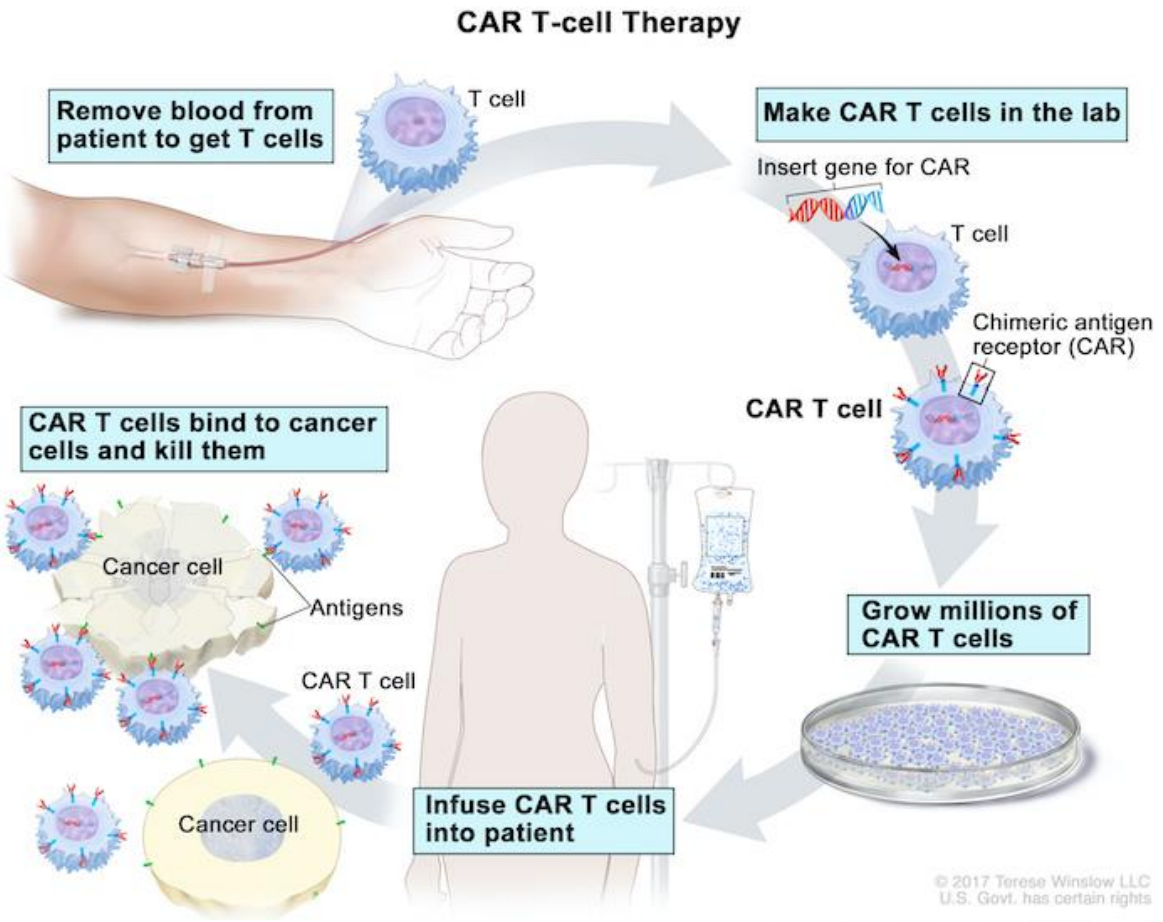
ALA Capital Raise History



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*

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

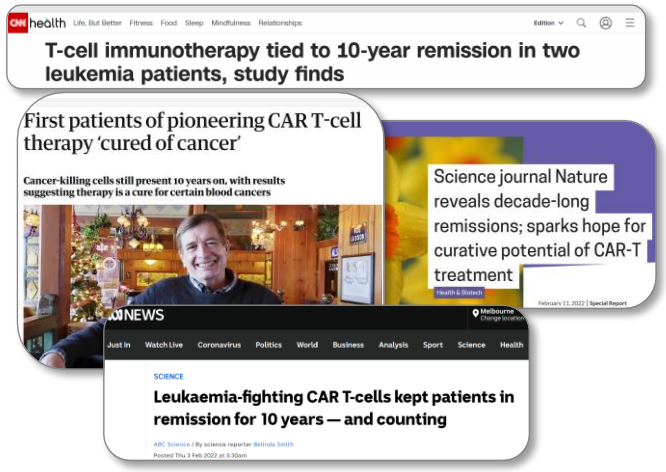


https://www.ohsu.edu/sites/default/files/2021-04/CAR%20TcellTherapy7-700px.jpg

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[1]

February 2022



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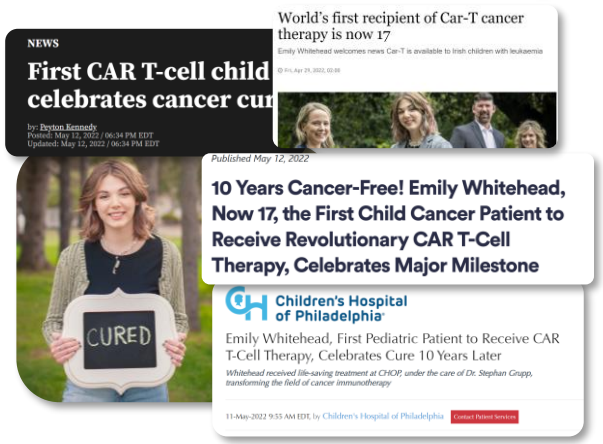

Product	Approval Year	2022 Revenue
YESCARTA® (axicabtagene ciloleucel)	2017	US$1160m[2]
KYMRIAH® (tisagenlecleucel)	2017	US$536m[3]
Abecma® (idecabtagene vicleucel)	2021	US$388m[4]

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*
3. *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.*

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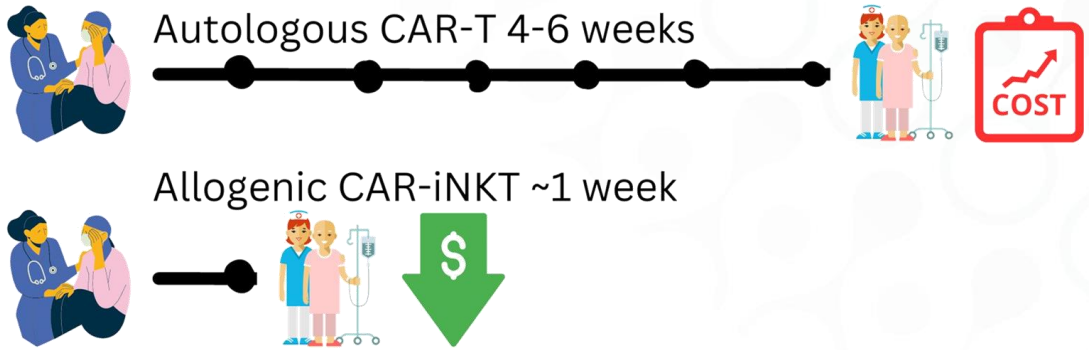
But…Manufacturing and Logistics Pose Major Challenges

- **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**

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

- **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)



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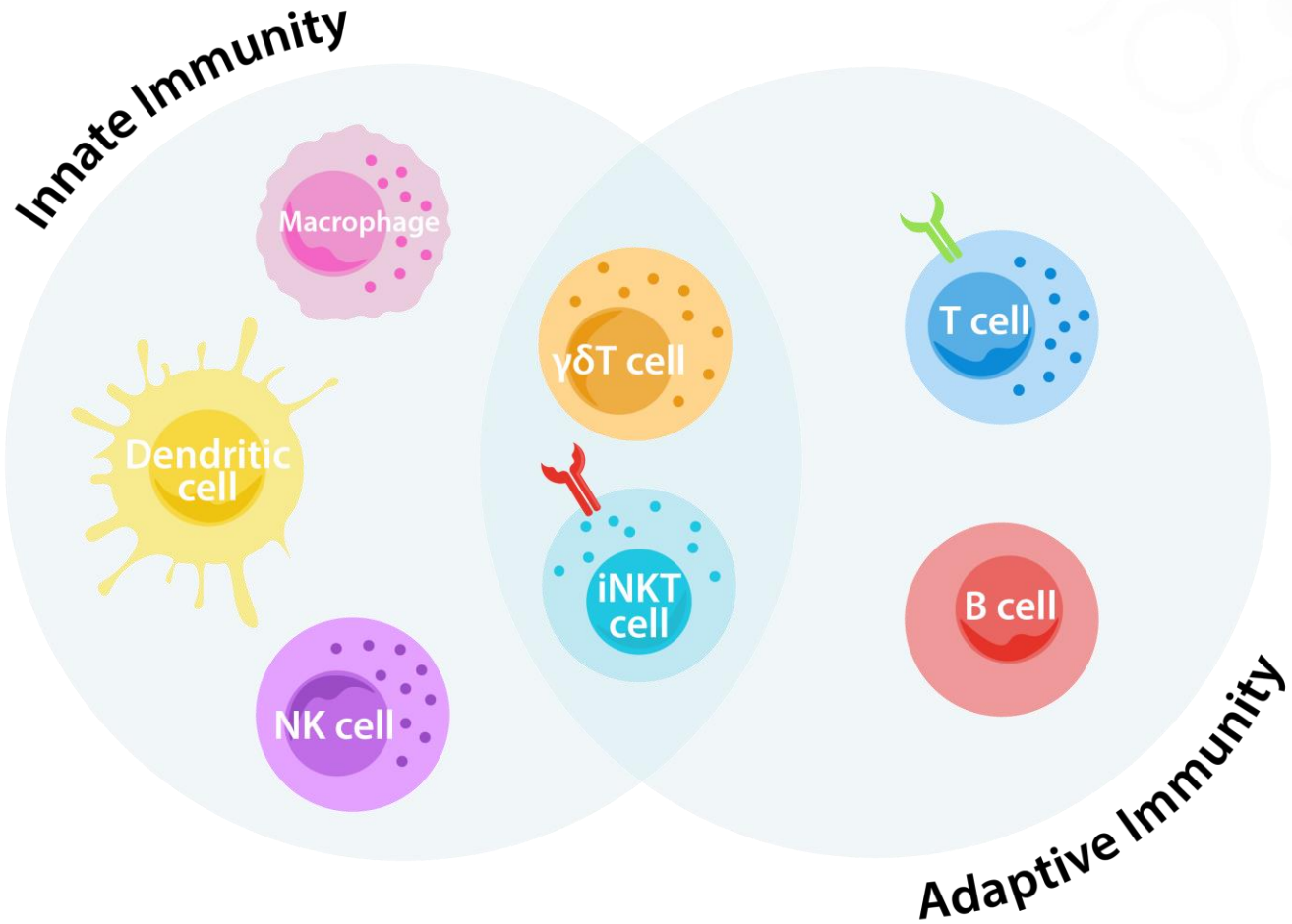
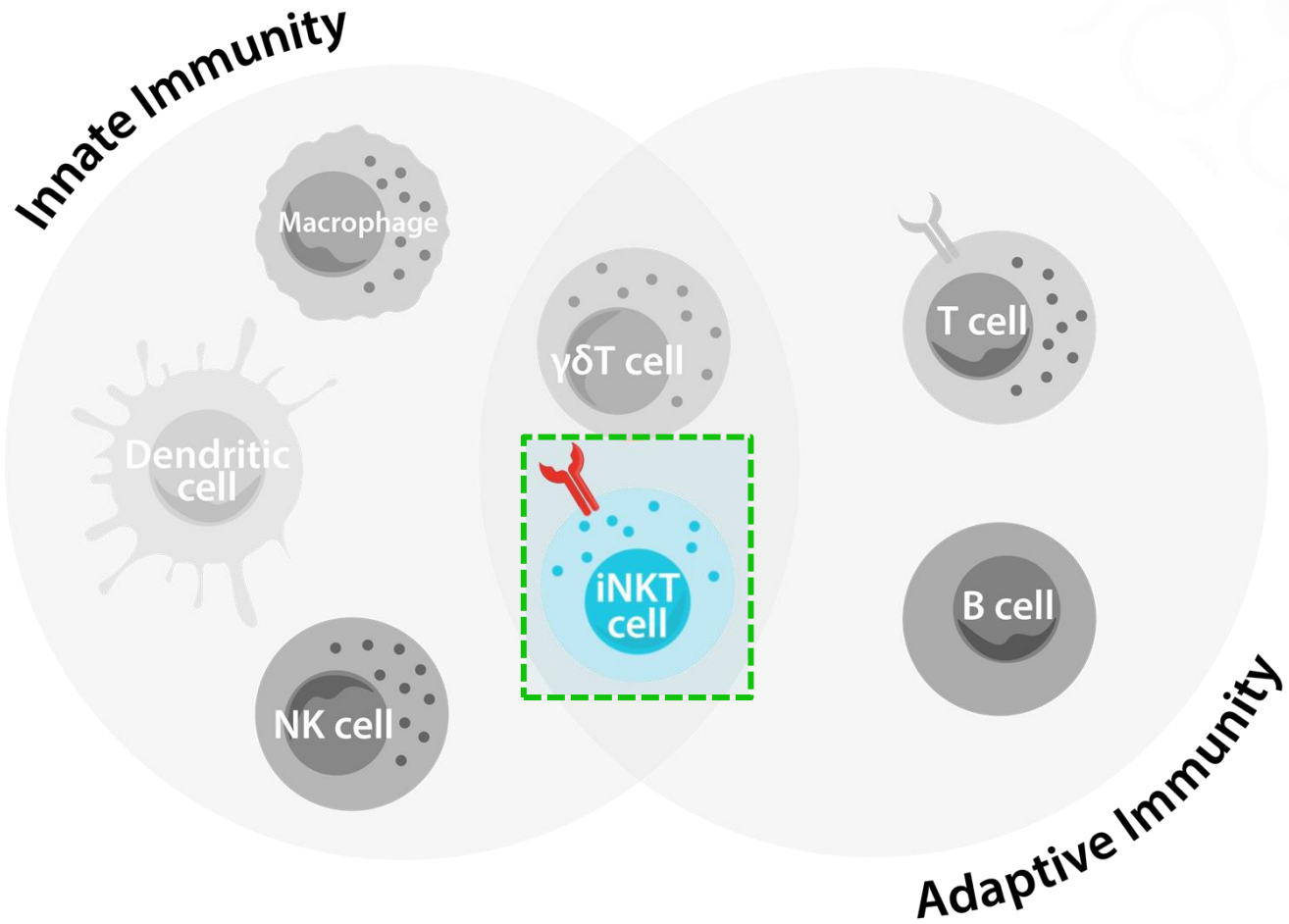
Introducing invariant Natural Killer (iNKT) Cells



Introducing iNKT Cells



- 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

TAM – Tumour associated macrophage
MDSC – myeloid derived suppressor cell

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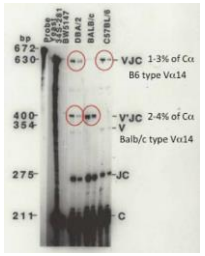
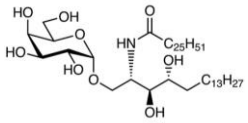
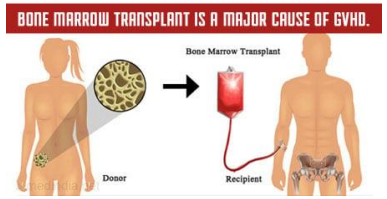
iNKT Cell Discovery and Therapeutic Evolution



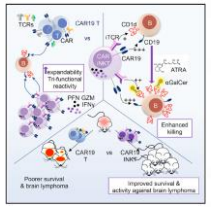
Murine iNKT cell discovery **1986**



MHC Class I-like CD1d ligand discovered – αGalCer **1997**



iNKT cells demonstrated to be protective against GVHD in humans **2012**



Arovella's iNKT cell platform published in Cancer Cell **2018**

Kite A GILEAD Company

APPIA BIO

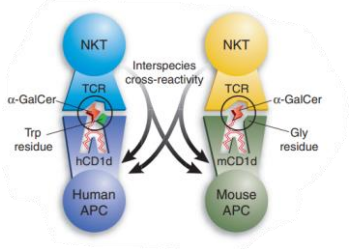
Appia exited stealth mode, raised $52m and entered into an $875m partnership with Kite Pharma **2021**

Imperial College London

Arovella licensed iNKT cell platform from ICL **2021**

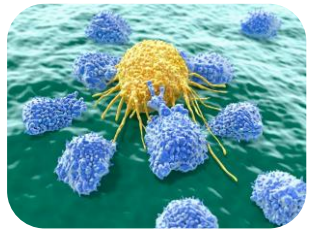
Timeline

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**

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Athenex

MiNK Therapeutics

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

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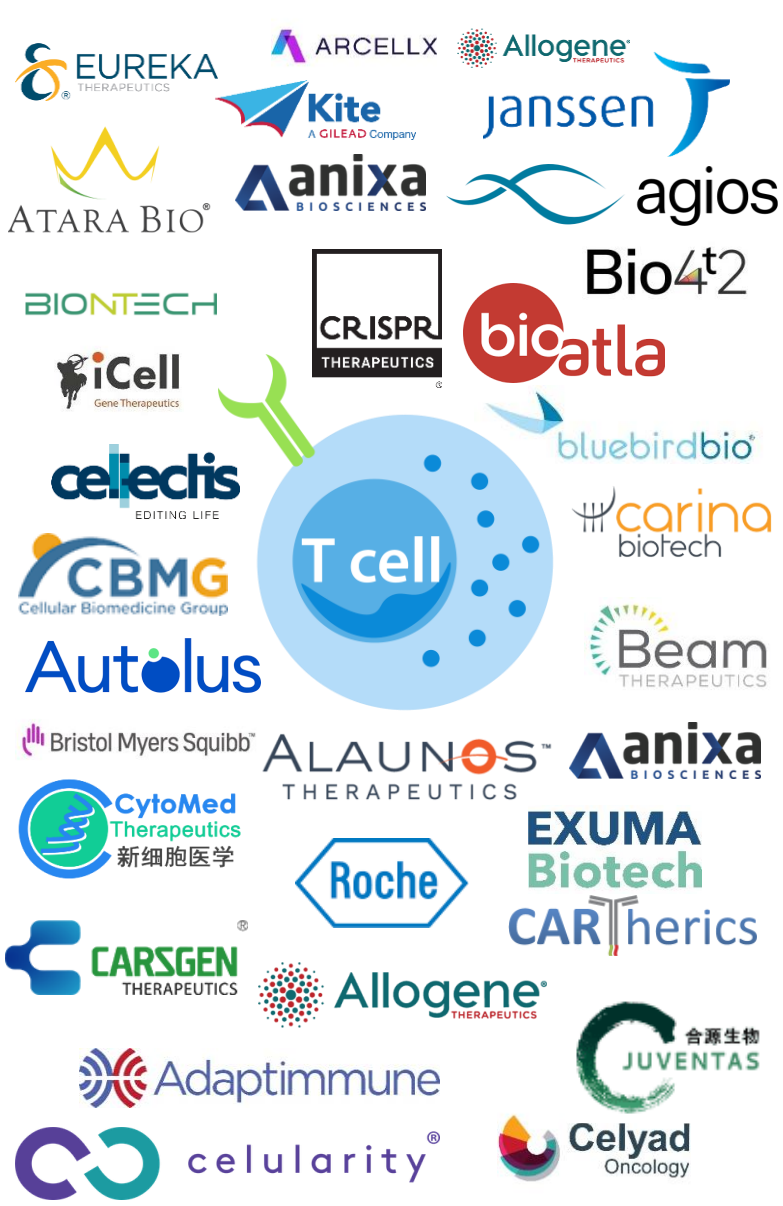
The Potential of CAR-iNKT Cells is Untapped



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)[1]
  - CD8+ T cells – 5-30% of PBMCs[1]
  - NK Cells – 5-20% of PBMCs[2]
  - iNKT cells – 0.01%-1.18% of PBMCs[3]
- For an autologous product targeting heamatological 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
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 Micribiol Immunol* 10.1007/s00430-016-0449-y

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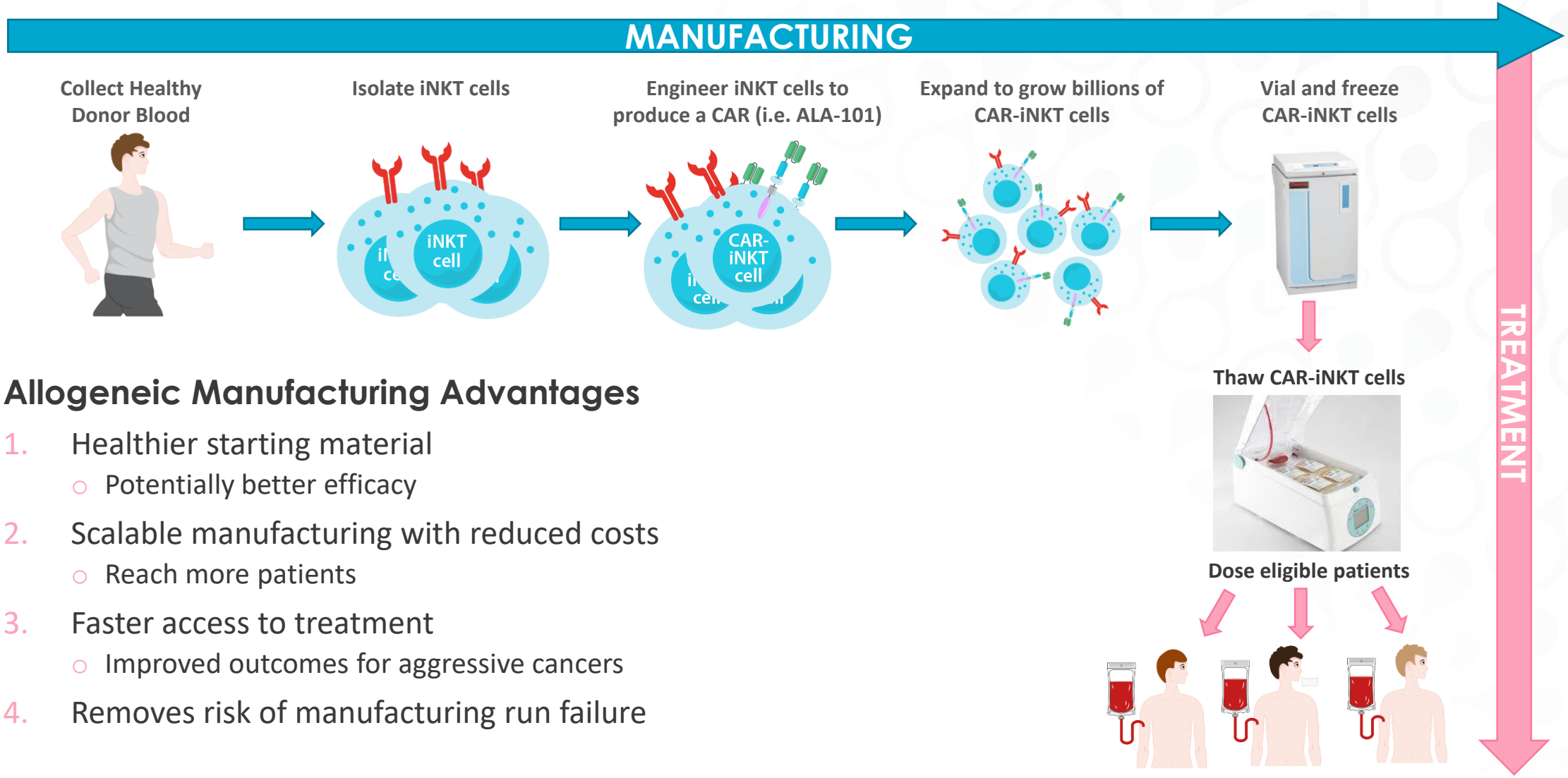
CAR-iNKT Cell Therapy Production Advantages



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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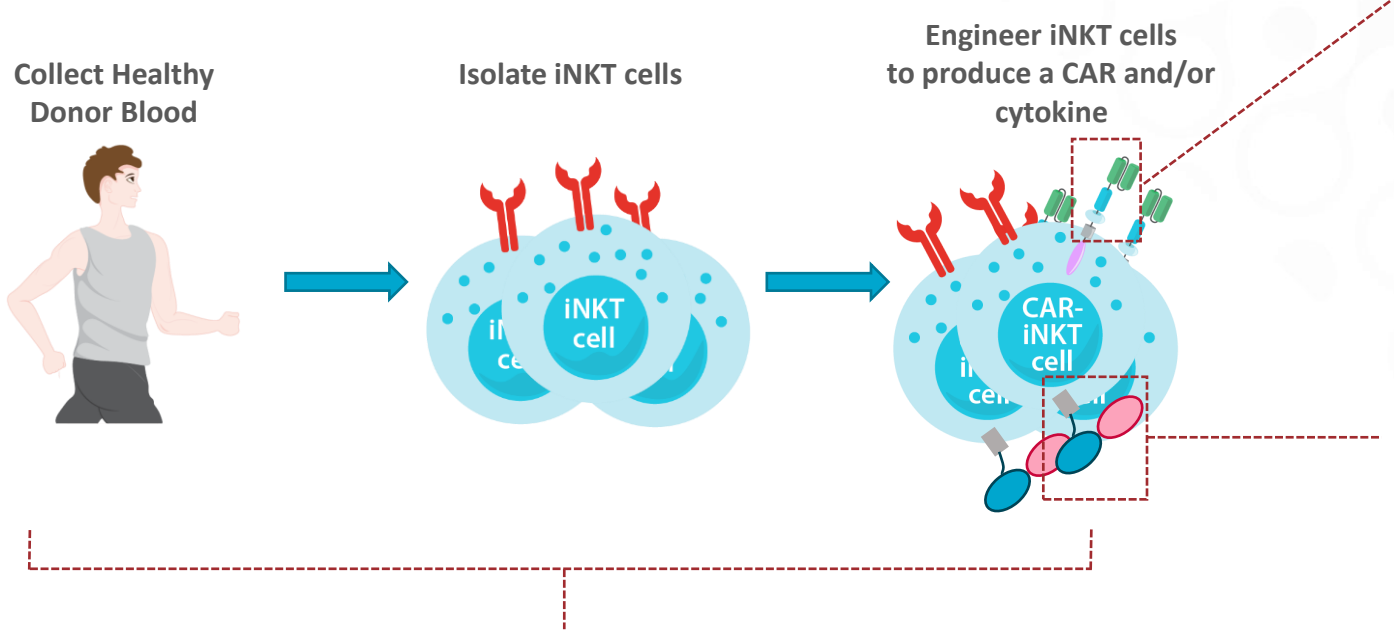
Arovella's Partnering Strategy In-licensing



NOVEL CARs

In-licence CARs to novel tumour targets across a range of blood cancers and solid tumours

E.g. DKK1 Novel Monoclonal Antibody, licenced from MD Anderson Cancer Centre in Dec 2021

Applicant: MD Anderson Cancer Center

Expiration: 2039

ENHANCE ACTIVITY IN SOLID TUMOURS

In licence novel technology that enhances the activity of iNKT cells, particularly in solid tumours

E.g. Patent covering the use of cytokines in iNKT cells for treatment of solid tumours, optioned from University of North Carolina in Dec 2022

Application: University of North Carolina

Expiration: 2041

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

Imperial College London

FOUNDATION PLATFORM

Novel, differentiated cell therapy platform targeting high unmet need diseases, with compelling pre-clinical data

E.g. Patent covering the manufacturing method to manufacture iNKT cells that express chimeric antigen receptors (CARs)

Applicant: Imperial College of Science Technology and Medicine

Expiration: 2038

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

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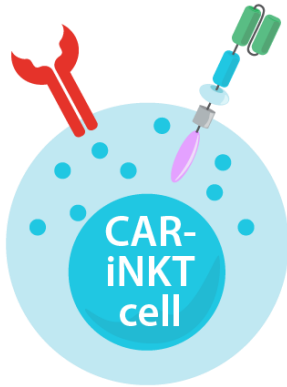
Arovella's Partnering Strategy Co-Development

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



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Imperial College London

Expecting *in vivo* data in H2 2023

- CF33 is an oncolytic virus that targets tumour cells[2]
- CF33 has been engineered to induce CD19 expression after tumour cells have been infected – onCARlytics[3]
- 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

Oncolytic virus CF33-CD19

IMUGENE Developing Cancer Immunotherapies

City of Hope

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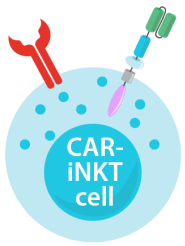
1. https://pubmed.ncbi.nlm.nih.gov/30300581/
2. https://pubmed.ncbi.nlm.nih.gov/32032721/
3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9126033/

Arovella's Potential Cancer Targets

CD19-CAR



CD19-CAR

Oncolytic virus
CF33-CD19

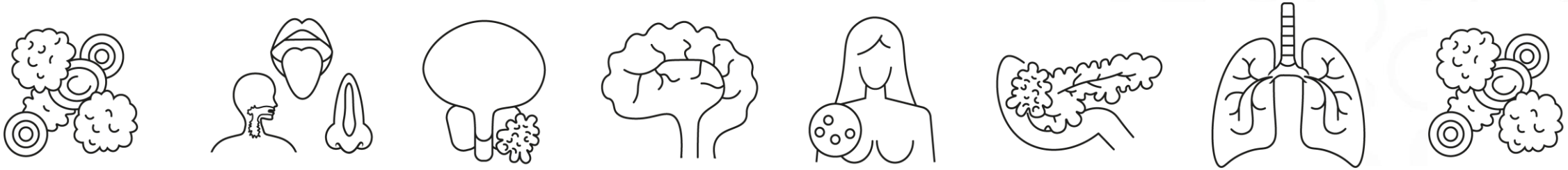
DKK1-CAR

ALA-101

ALA-101 + onCARlytics

ALA-104

Cytokine Technology



Non-Hodgkin's Lymphoma	Head and Neck Cancer	Prostate Cancer	Brain Metastases	Triple negative breast cancer	Pancreatic Cancer	Lung Cancer	Multiple Myeloma

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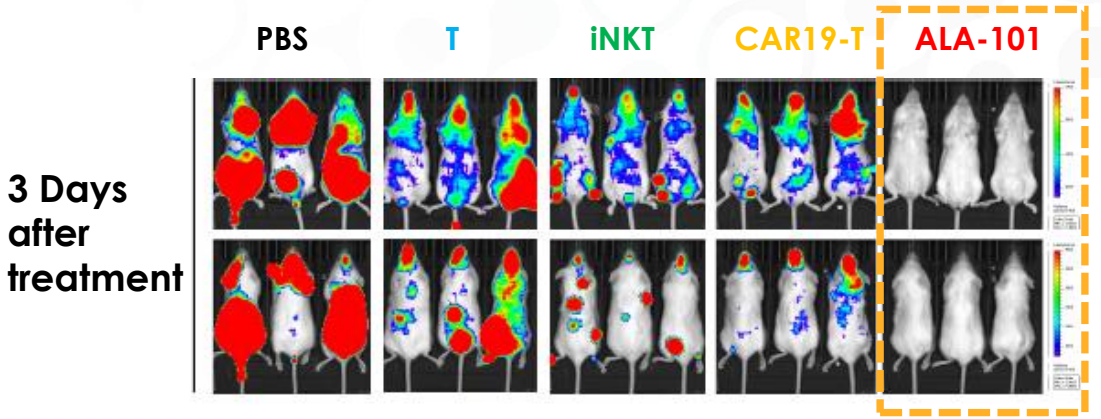
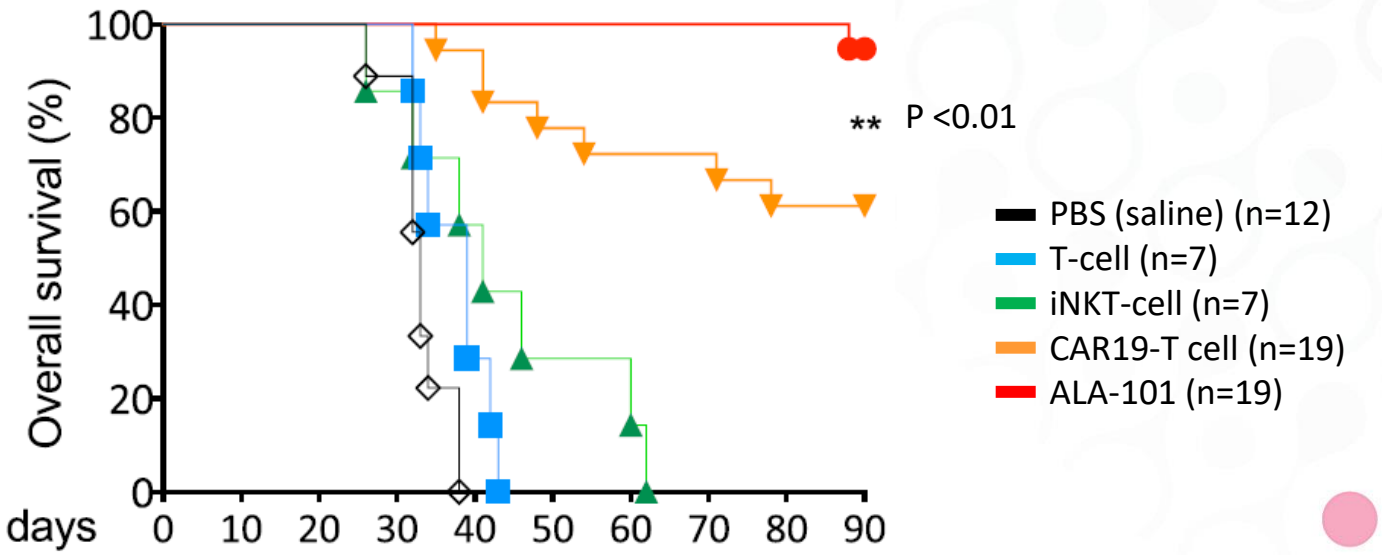
ALA-101: Superior Activity Over CAR-T Cells

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**



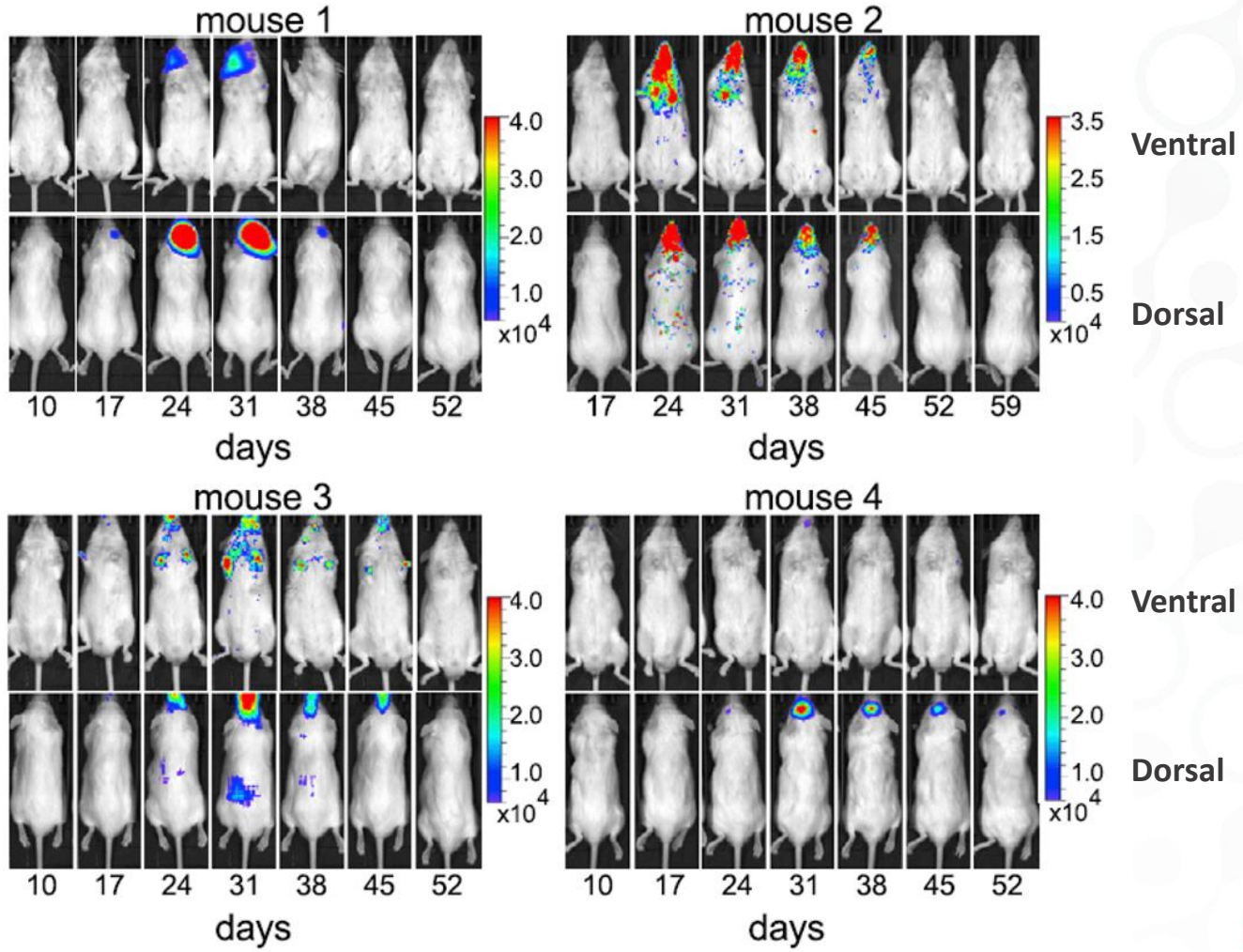


Rotolo *et al.*, Cancer Cell (2018)

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

	June 2023	December 2023	June 2024
ALA-101	▪ 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	▪ Complete cGMP manufacture for phase I clinical trials ▪ Complete preparatory activities for phase I study, including submission of regulatory dossier.	
iNKT Cell Therapy Platform	▪ 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)	▪ Initiate proof-of-concept testing for novel CARs and/or cytokine technology to expand iNKT platform for treatment of solid tumours	

DLTs – Dose Limiting Toxicities
cGMP – Current Good Manufacturing Practice

Recent Cell Therapy Transactions

Date	Type of deal	Acquirer/Licensee	Target/Licensor	Stage	Upfront (US$M)	Milestones (US$M)	Total deal value (US$M)
May-23	License	janssen	CBMG Cellular Biomedicine Group	Phase Ib	$245	undisclosed	
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™	Preclinical	$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	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
				Mean	**$146**	**$208**	**$364**

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
Mobile: +61 403 468 187

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