ardvella
THERAPEUTICS

ASX:ALA

Investor Presentation

January 2023

Disclaimer

1. The information in this presentation does not constitute personal investment advice. The presentation is not intended to be comprehensive or provide all information required by investors to make an informed decision on any investment in Arovella Therapeutics Limited (**Company**).
In preparing this presentation, the Company did not take into account the investment objectives, financial situation and particular needs of any particular investor.
2. Further advice should be obtained from a professional investment adviser before taking any action on any information dealt with in the presentation. Those acting upon any information without advice do so entirely at their own risk.
3. Whilst this presentation is based on information from sources which are considered reliable, no representation or warranty, express or implied, is made or given by or on behalf of the Company, any of its directors, or any other person about the accuracy, completeness or fairness of the information or opinions contained in this presentation. No responsibility or liability is accepted by any of them for that information or those opinions or for any errors, omissions, misstatements (negligent or otherwise) or for any communication written or otherwise, contained or referred to in this presentation.
4. Neither the Company nor any of its directors, officers, employees, advisers, associated persons or subsidiaries are liable for any direct, indirect or consequential loss or damage suffered by any person as a result of relying upon any statement in this presentation or any document supplied with this presentation, or by any future communications in connection with those documents and all of those losses and damages are expressly disclaimed.
5. Any opinions expressed reflect the Company's position at the date of this presentation and are subject to change.
6. This document does not constitute an offer to sell, or a solicitation of an offer to buy, securities in the United States or any other jurisdiction in which it would be unlawful. In particular, the New Shares and Options have not been, and will not be, registered under the US Securities Act of 1933 (the "US Securities Act") and may not be offered or sold in the United States except in transactions exempt from, or not subject to, the registration requirements of the US Securities Act and applicable US state securities laws. The distribution of this presentation in jurisdictions outside Australia may be restricted by law and any such restrictions should be observed.
7. The New Shares and Options will be offered and sold in the United States only to (i) institutional accredited investors (as defined in Rule 501(a)(1), (2), (3) and (7) under the US Securities Act); and (ii)dealers or other professional fiduciaries organized or incorporated in the United States that are acting for a discretionary or similar account (other than an estate or trust) held for the benefit or account of persons that are not US persons and for which they exercise investment discretion, within the meaning of Rule 902(k)(2)(i) of Regulation S under the US Securities Act.

arovella THERAPEUTICS

Arovella Therapeutics Highlights

Allogeneic iNKT Cell Platform

Arovella is developing off-the-shelf iNKT cell therapies for CD19 expressing lymphomas and solid tumors, and DKK1 producing cancers

World Leading Partners

Arovella's technologies are licensed from **Imperial College London** and **MD Anderson Cancer Center.** Arovella has an ongoing collaboration with **Imugene**

Strong Leadership Group

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

Data Driven

Arovella uses data to drive decision making for its key assets and clinical indications

Acquiring New Technologies

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, and the only company developing a CAR targeting a DKK1-peptide

arovella THERAPEUTICS

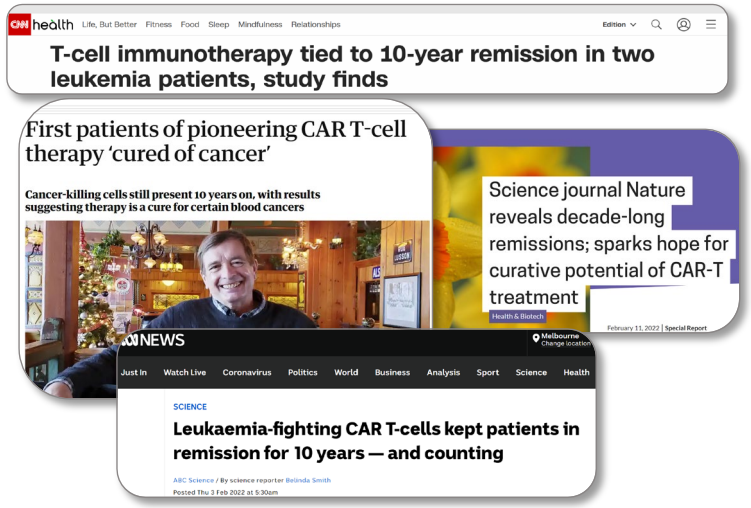
Cell Therapy Has Revolutionized Blood Cancer Treatment

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

BUT…….

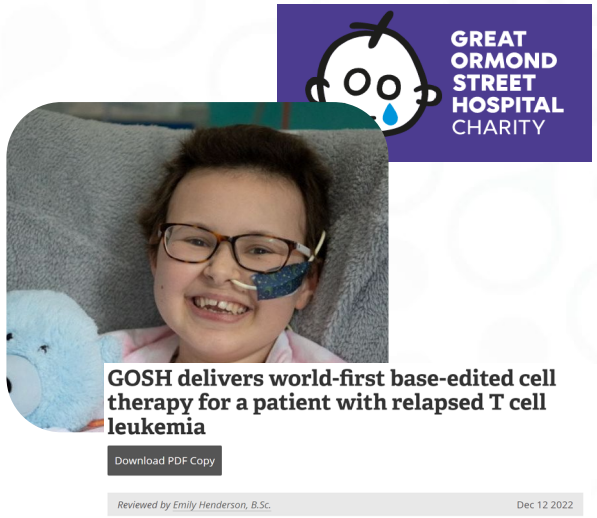
- Manufacturing, logistics and access have prevented broader patient uptake
- **Arovella's CAR-iNKT cell platform** addresses these challenges and has the potential for **improved efficacy**

February 2022



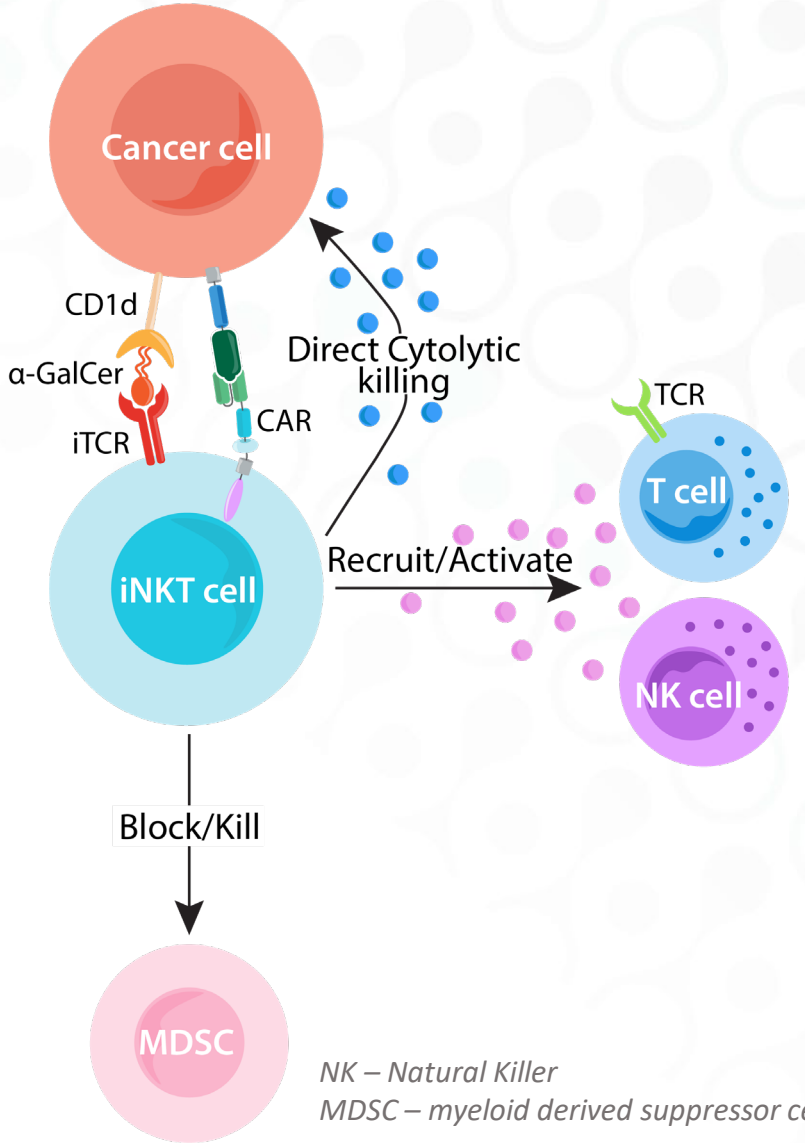
May 2022

December 2022



iNKT Cells are Primed to Kill Cancer

- invariant Natural Killer T (iNKT) cells naturally target and kill cancer cells[1]
- The invariant T Cell Receptor (TCR) does not change between people and iNKT cells are protective against graft versus host disease (GVHD) [2,3]
- Can be administered “off-the-shelf”
- Shape the tumor microenvironment, promoting tumor destruction[4]
- Recruit other components of the immune system to attack cancer cells[5]
- Addition of a Chimeric Antigen Receptor (CAR) makes them dual targeting, enhancing cytotoxicity[6]
- CAR-iNKT cells mount a rapid response and display robust tumor killing *in vivo*[6]



NK – Natural Killer
MDSC – myeloid derived suppressor cell

1. *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6036112/*
2. *https://pubmed.ncbi.nlm.nih.gov/28824628/*
3. *https://ashpublications.org/blood/article/127/14/1828/34747/Larger-number-of-invariant-natural-killer-T-cells*
4. *https://www.frontiersin.org/articles/10.3389/fimmu.2022.999549/full*
5. *https://link.springer.com/article/10.1007/s00441-010-1023-3*
6. *https://pubmed.ncbi.nlm.nih.gov/30300581/*

arovella THERAPEUTICS

CAR-iNKT Cell Therapy is a Superior Cell Therapy Platform

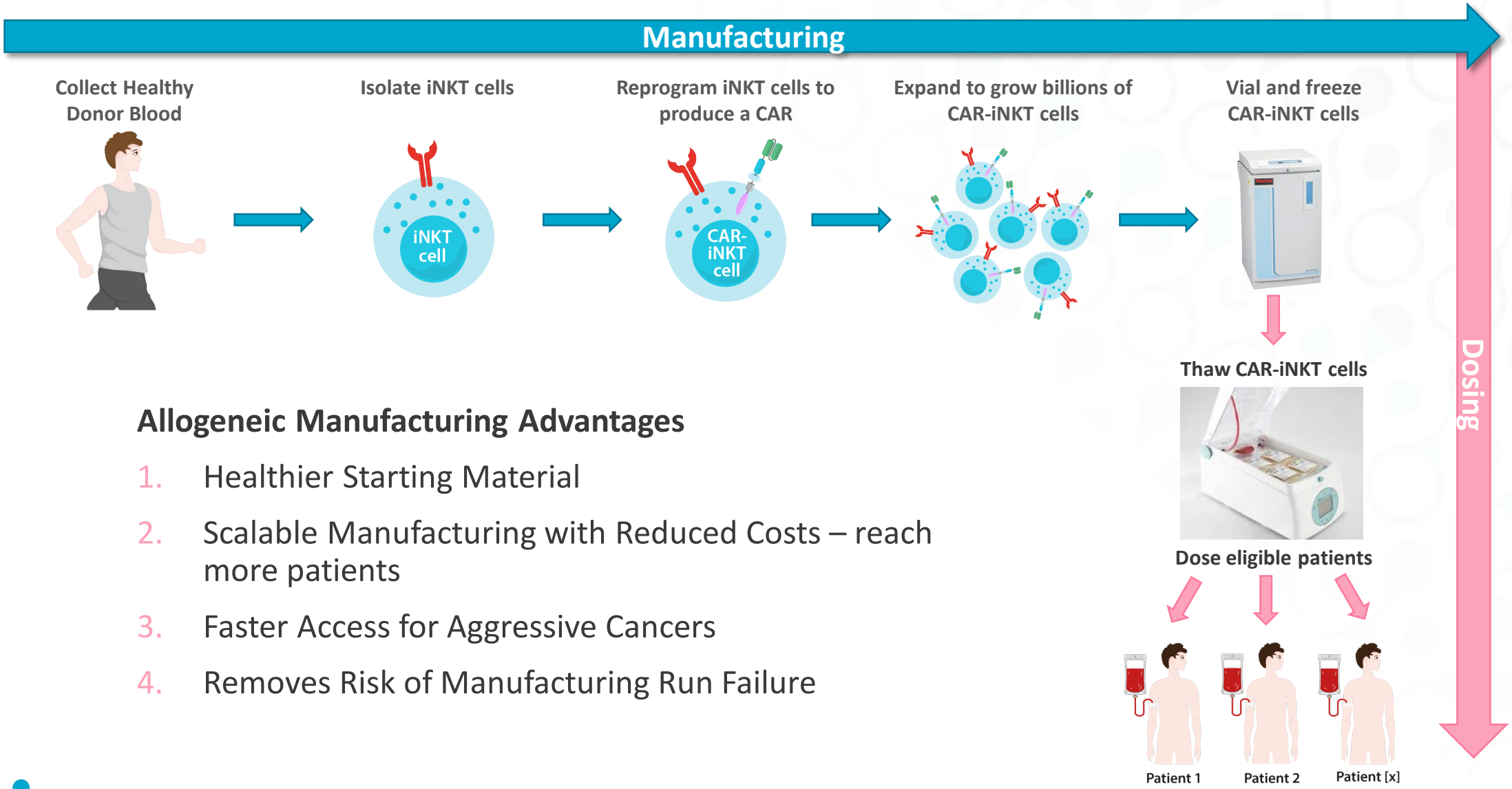
iNKT cells are a subpopulation of T cells that have NK cells properties

	APPROVED CAR-T CELLS	ALLOGENEIC CAR-T CELLS	ALLOGENEIC CAR-NK CELLS	CAR-iNKT CELLS
Multiple Cancer Targeting Mechanisms (iTCR-CD1d mediated)	✗	✗	✗	✓
T and NK cell mechanisms of killing	✗	✗	✗	✓
Naturally suppress GvHD	✗	✗	✗	✓
Allogeneic, 'off-the-shelf' dosing	✗	✓	✓	✓
Gene editing not required for allogeneic cells	✗	✗	✓	✓

iTCR – invariant T Cell Receptor; CAR – Chimeric Antigen Receptor; NK – Natural Killer; iNKT – invariant Natural Killer T; GvHD – Graft Versus Host Disease

arovella THERAPEUTICS

CAR-iNKT Cell Therapy Production Advantages



Allogeneic Manufacturing Advantages

1. Healthier Starting Material
2. Scalable Manufacturing with Reduced Costs – reach more patients
3. Faster Access for Aggressive Cancers
4. Removes Risk of Manufacturing Run Failure

arovella THERAPEUTICS

Arovella Therapeutics Cell Therapy Pipeline

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 Tumors			
DKK1-CAR-iNKT **(ALA-104)**		Multiple Myeloma			
		TNBC			
		NSCLC			
		Pancreatic			

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

CAR19-iNKT (**ALA-101**)

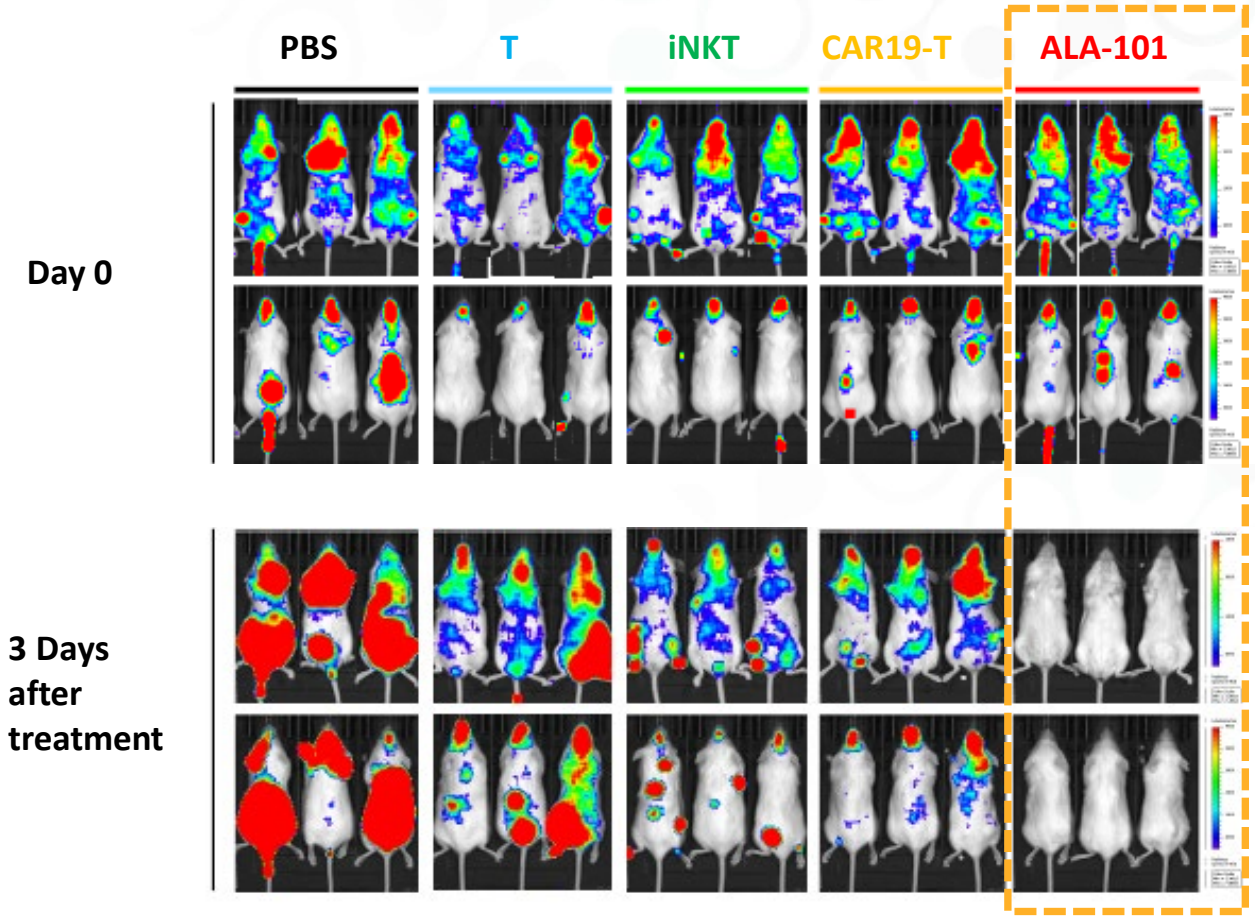
An off-the-shelf cell therapy for CD19 expressing cancers

arovella THERAPEUTICS

ALA-101: Enhanced Tumor Killing *In Vivo*

ALA-101 rapidly eradicates tumor cells in mice

- Tumor 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 three days, ALA-101 resulted in significant regression of tumor cells
- In all other treatments, we observed strong tumor cell persistence
- ALA-101 displays swift action

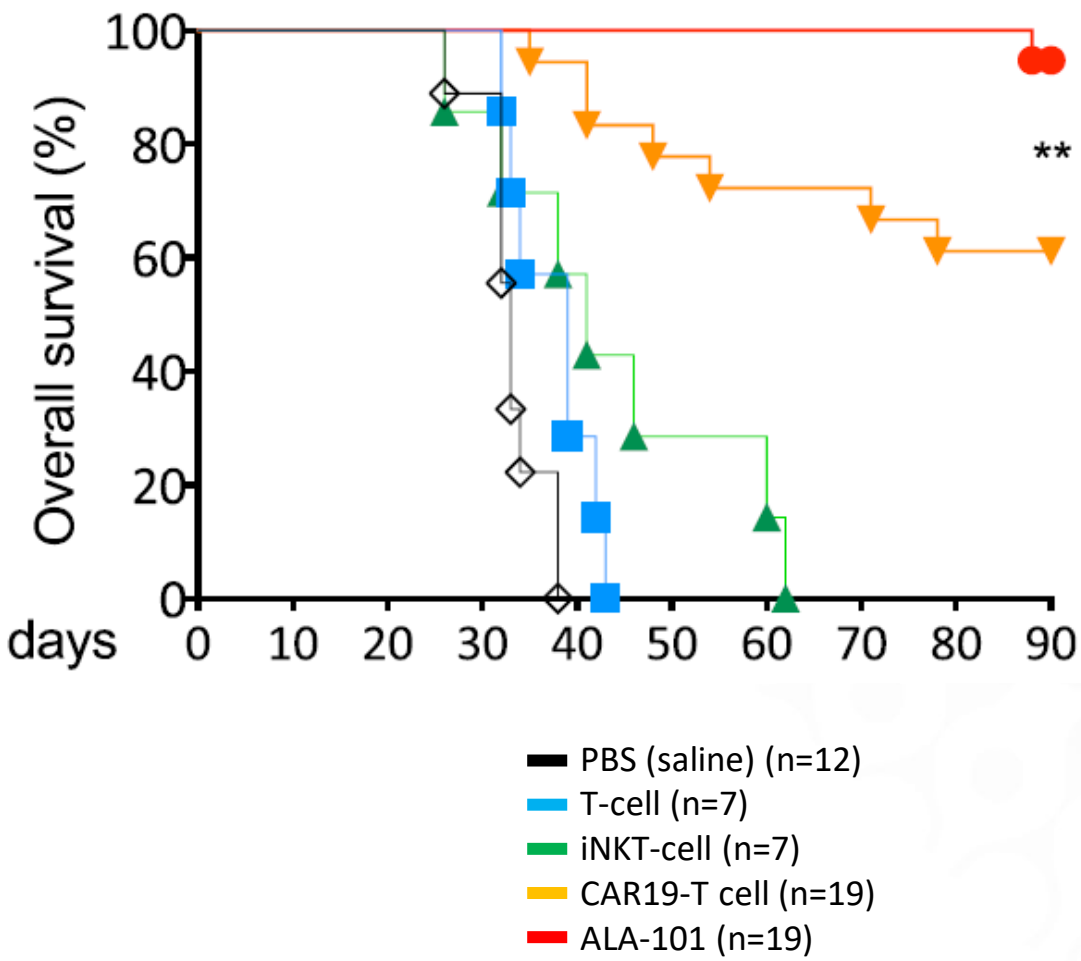


Rotolo *et al.*, Cancer Cell (2018)

ALA-101: Superior Animal Survival Over CAR-T Cells

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

- Tumor 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**

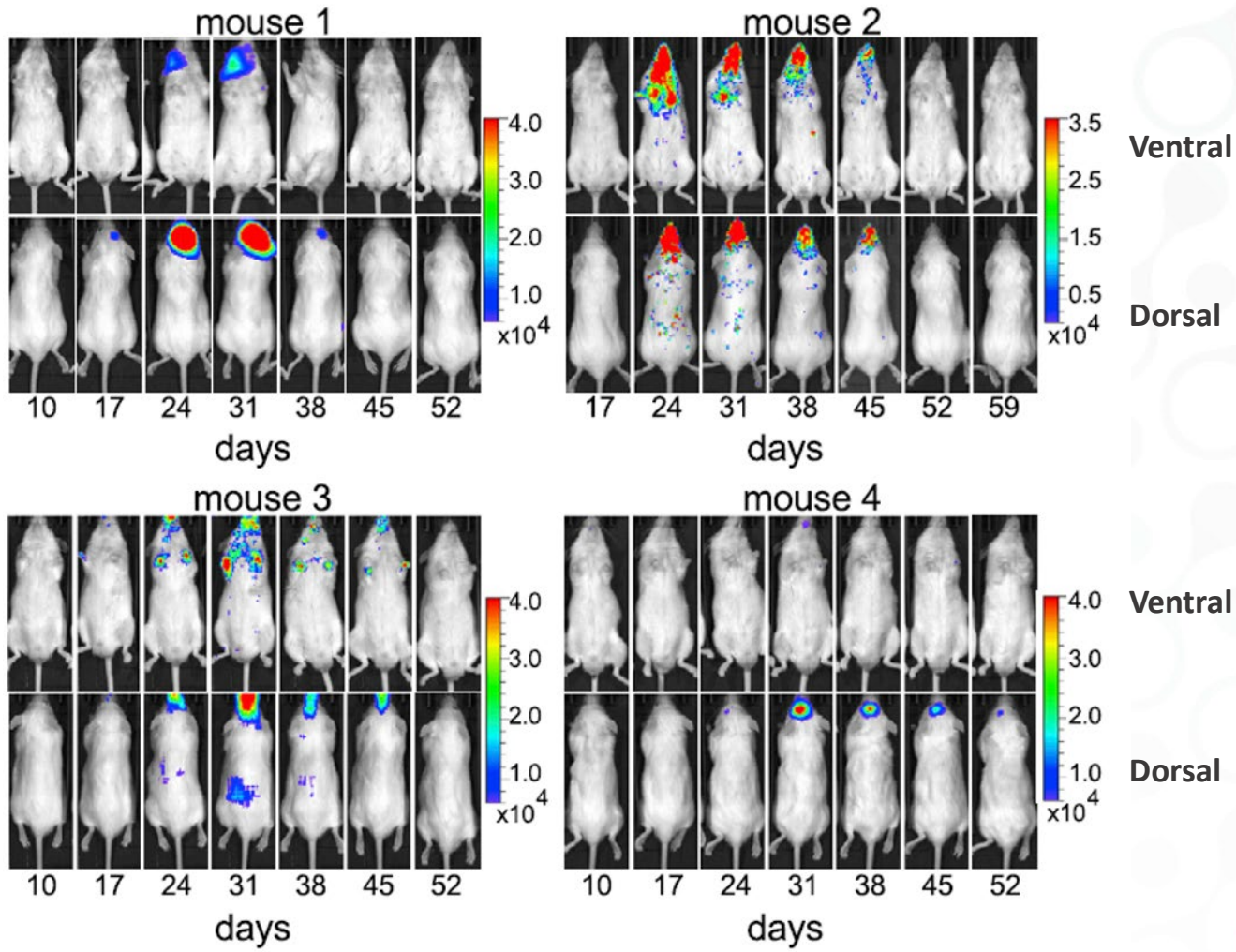


Rotolo *et al.*, Cancer Cell (2018)

ALA-101: Spontaneous Secondary Remission

ALA-101 activity may persist to eradicate tumor 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 infers that CAR19-iNKT cells can survive and continue to protect against cancer cells *in vivo*
- Potential to use ALA-101 to treat central nervous system lymphoma or brain metastases



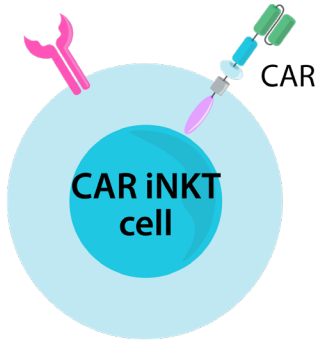
Rotolo *et al.*, Cancer Cell (2018)

ALA-101 + CF33-CD19

An off-the-shelf cell therapy and oncolytic virus combination to mark and destroy solid tumors

Combining ALA-101 and CF33-CD19 (onCARlytics)

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



arovella THERAPEUTICS

Imperial College London

- CF33 is an oncolytic virus that targets tumor cells and not healthy cells[2]
- CF33 has been further engineered to induce CD19 expression after tumor cells have been infected – onCARlytics[3]
- Phase 1 trials for CF33 commenced October 2021 with CHECKvacc and May 2022 with VAXINIA

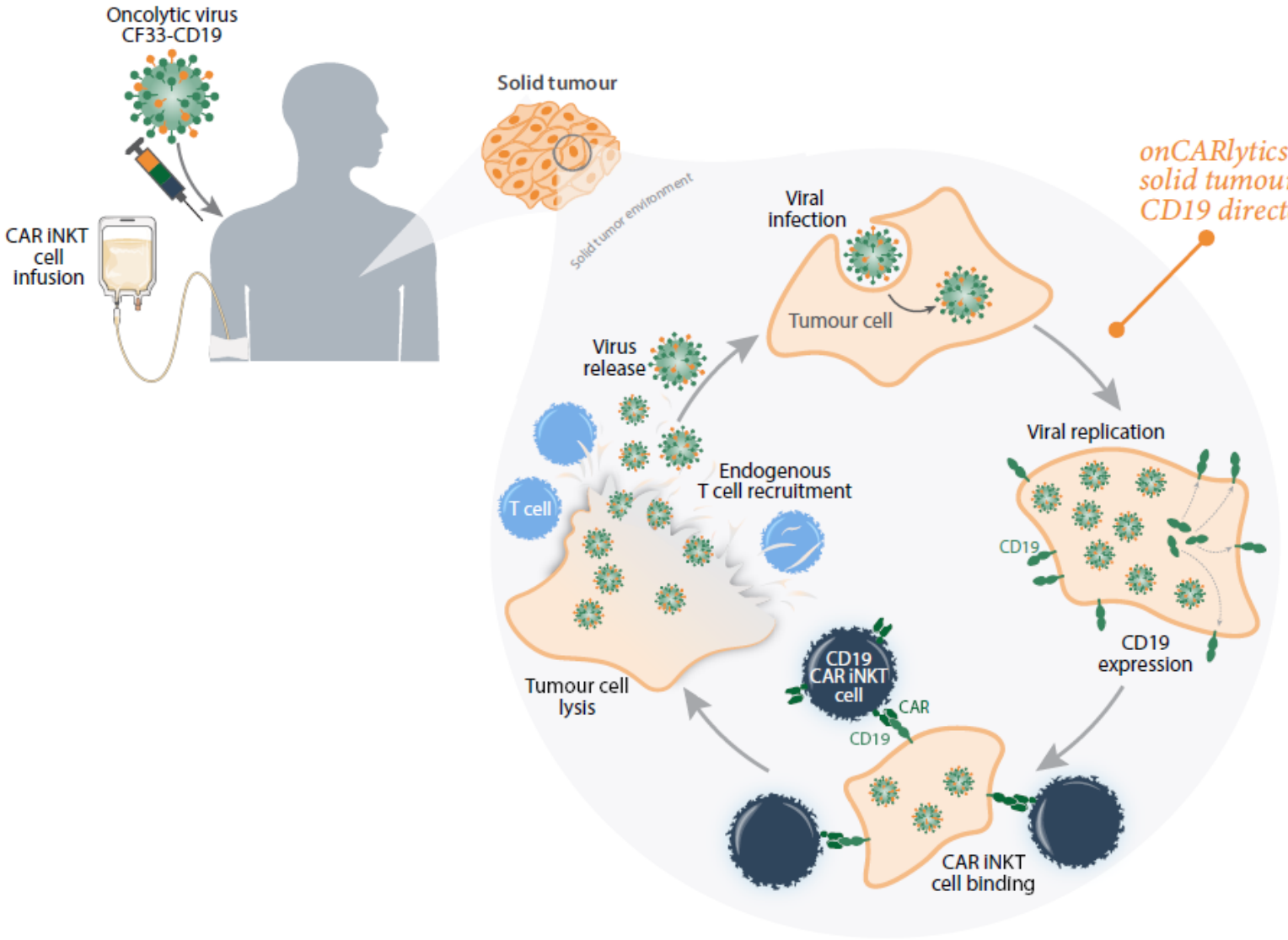
IMUGENE
Developing Cancer Immunotherapies

City of Hope

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/*

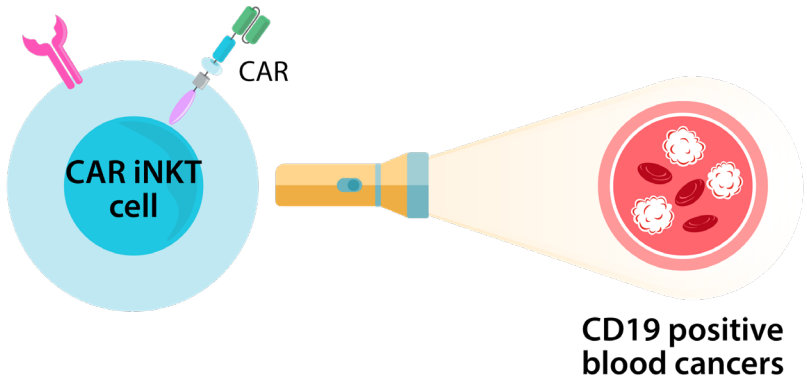
arovella THERAPEUTICS

ALA-101 + onCARlytics Mechanism of Action

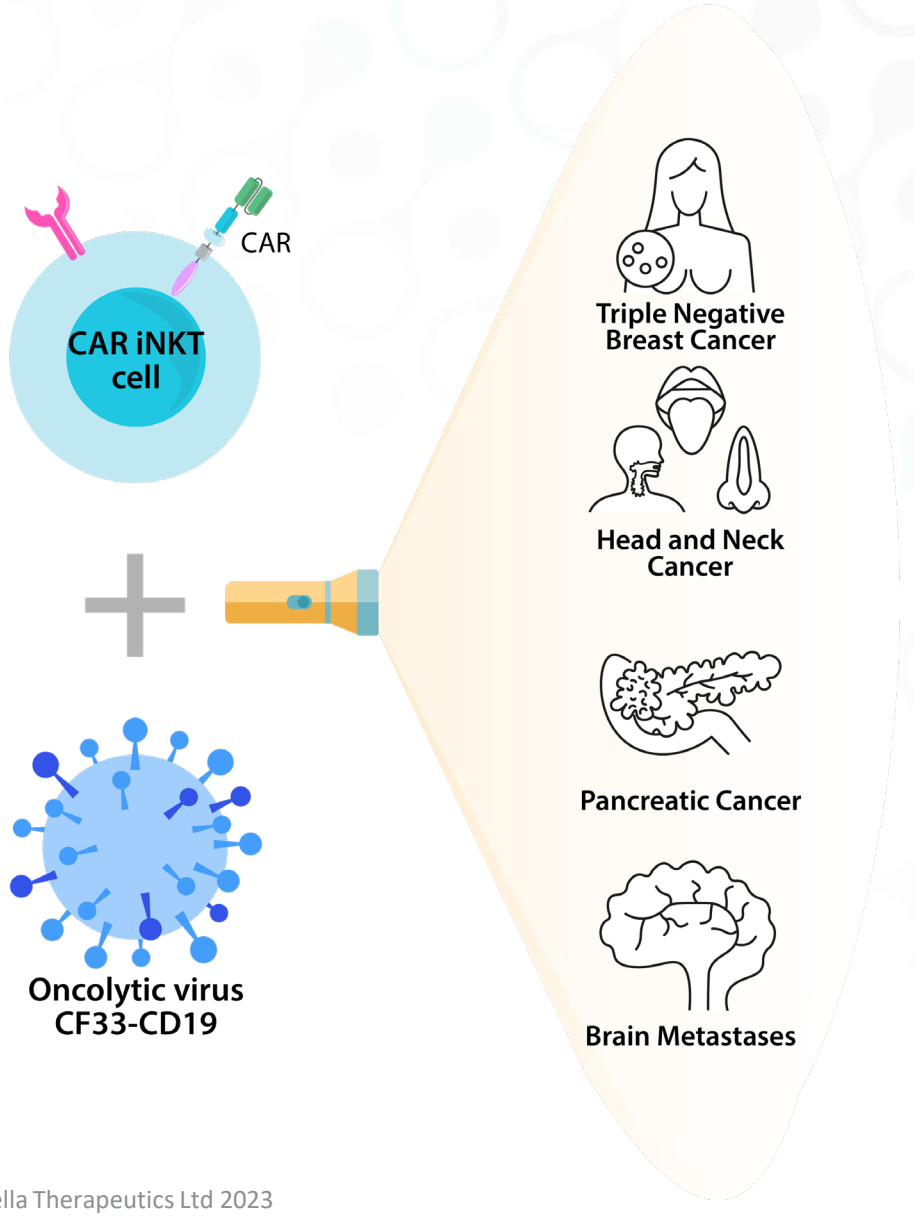


1. OnCARlytics infects tumour cells
2. Virus replication and production of CF33-CD19 on the cell surface enabling CD19 targeting
3. Tumour cell lysis leads to viral particle release and the combination promotes endogenous immune cell recruitment to tumours
4. Released viral particles re-initiate virus infection of surrounding tumour cells.

Expanding ALA-101's Utility by Combining with onCARlytics



- We expect ALA-101 to be effective against blood cancers that naturally express CD19
- Combining onCARlytics with ALA-101 cells opens up the possibility of treating a range of solid tumors



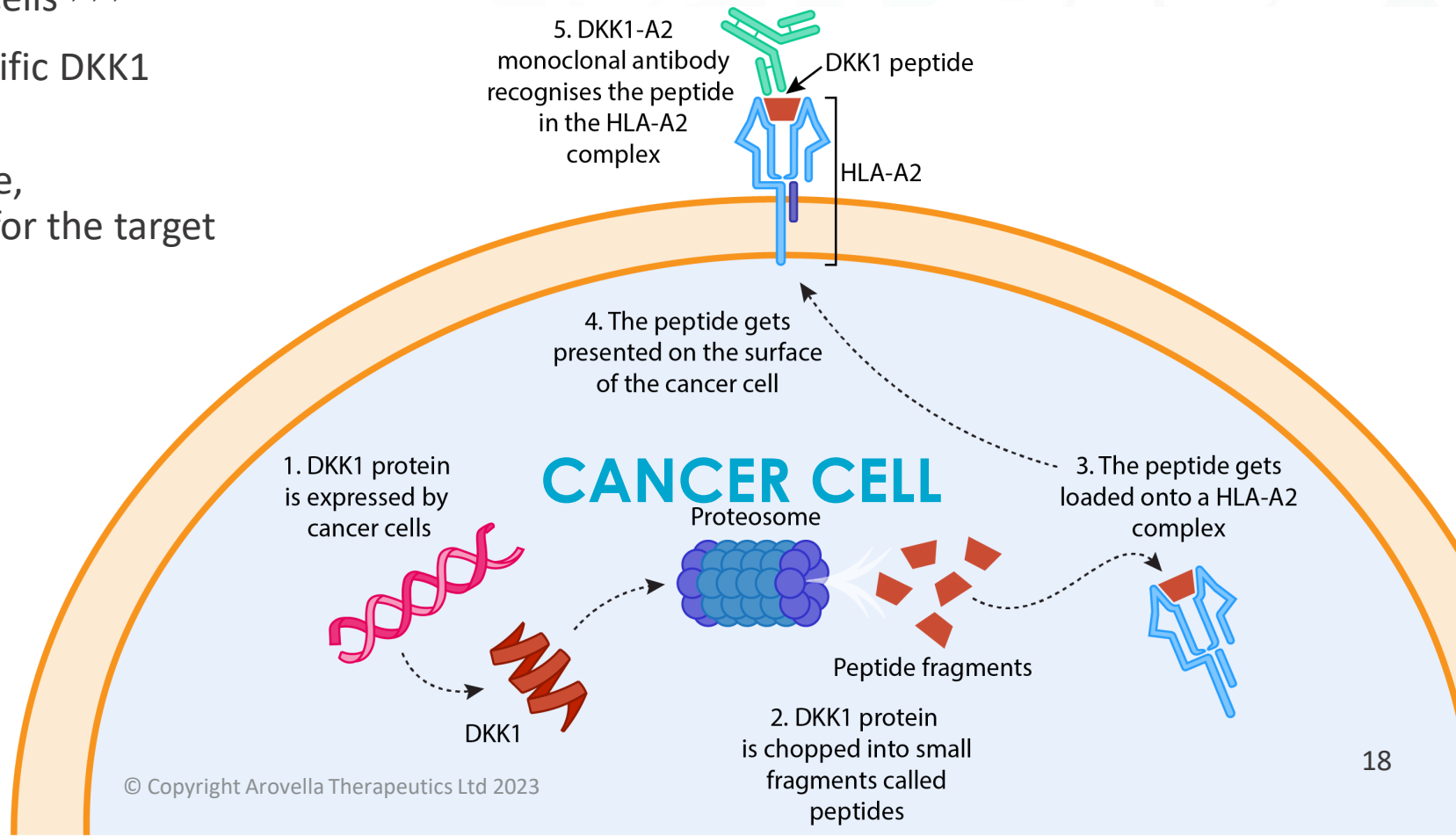
DKK1-CAR-iNKT Cells (**ALA-104**)

An off-the-shelf cell therapy for multiple myeloma and potentially solid tumors

arovella THERAPEUTICS

DKK1 is a Novel Cancer Target

- DKK1 is a secreted protein that functions as a negative regulator of the WNT signaling pathway[1]
- DKK1 is overexpressed in numerous cancer types and DKK1 peptides are loaded onto immune complexes and presented at the surface of cancer cells[2,3,4,5]
- Arovella's DKK1 mAb/CAR targets a specific DKK1 peptide in an HLA-A2 complex
- ~40-50% of the population is HLA-A2 +ve, representing a potentially large market for the target

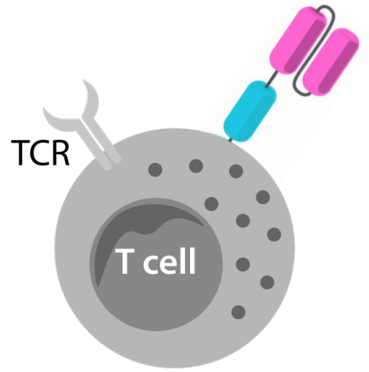


1. https://www.nature.com/articles/1207892
2. https://www.nature.com/articles/s41388-021-01860-z
3. https://link.springer.com/article/10.1007/s10585-018-9937-3
4. https://link.springer.com/article/10.1007/s00432-019-03114-8
5. https://www.nature.com/articles/s41392-019-0082-5#article-info

The DKK1 CAR has been Validated in CAR-T Cells

- Demonstrated activity of the DKK1 peptide-targeting mAb against multiple myeloma and breast cancer
- DKK1-CAR-T cells show potent activity against both blood cancers and solid tumors (unpublished)
- We are combining the DKK1-CAR with the iNKT cell therapy platform (ALA-104)
- ALA-104 initial development is focused on multiple myeloma, followed by expansion into other solid tumors expressing DKK1 and potentially CD1d

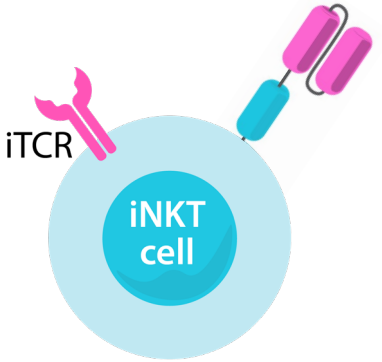
Already Completed



DKK1-CAR-T cells

Multiple Myeloma ✓
Pancreatic Cancer ✓
Lung Cancer ✓
Breast Cancer ✓

In Progress



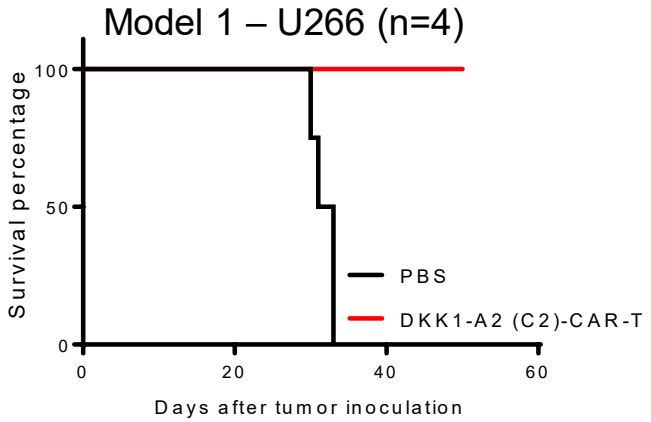
DKK1-CAR-iNKT cells

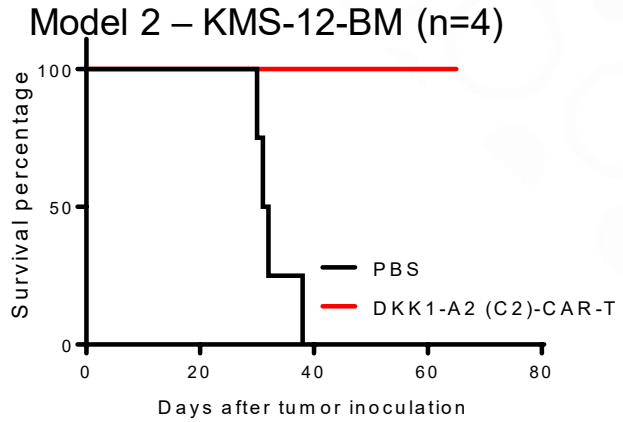
Multiple Myeloma
Pancreatic Cancer
Lung Cancer
Breast Cancer

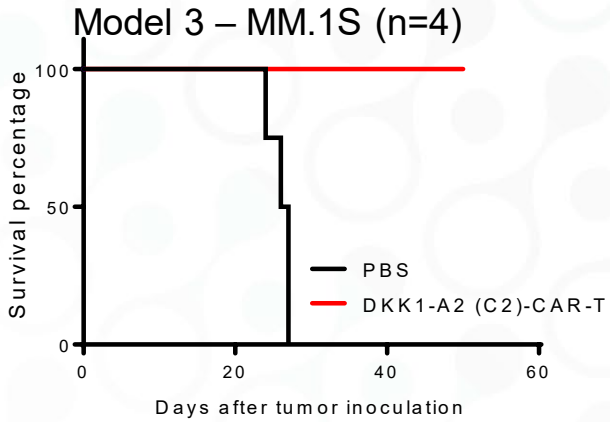
arovella THERAPEUTICS

DKK1-CAR-T Cell Activity Against Multiple Myeloma

DKK1-CAR-T cells were tested in three different animal models of multiple myeloma, displaying robust activity in all standard models







- All treated mice were alive at 50-60 days, while untreated mice succumbed to the cancer at 30-40 days
- Multiple myeloma cells also express CD1d, so engineering DKK1-CAR into iNKT cells makes them dual targeting[1,2,3]

1. *https://pubmed.ncbi.nlm.nih.gov/19056691/*
2. *https://pubmed.ncbi.nlm.nih.gov/18980990/*
3. *https://pubmed.ncbi.nlm.nih.gov/12796469/*

arovella THERAPEUTICS

DKK1-CAR-T Preclinical Safety

Data demonstrates:

- They only kill cells that have the target on their surface
- They do not kill healthy blood cells
- They do not cause weight loss when administered to mice
- The DKK1 mAb non-specifically targeted only 1 out of 35 tissues tested (tonsil)

Arovella is confirming:

- That the DKK1 technology does not target or attack healthy cells
- The ability to combine DKK1-CAR with the iNKT cell therapy platform

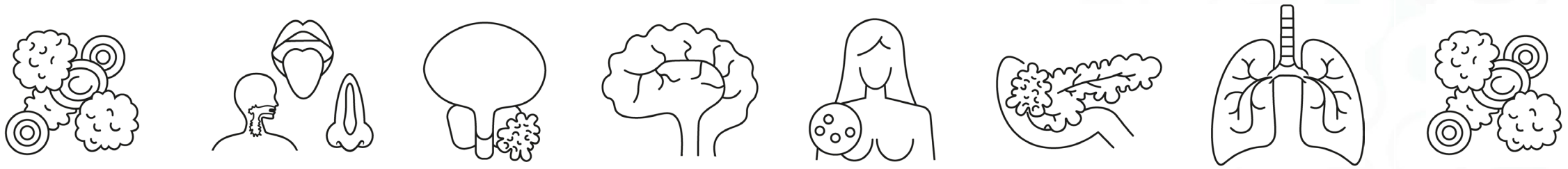
arovella
THERAPEUTICS

Arovella's Potential Cancer Targets

ALA-101

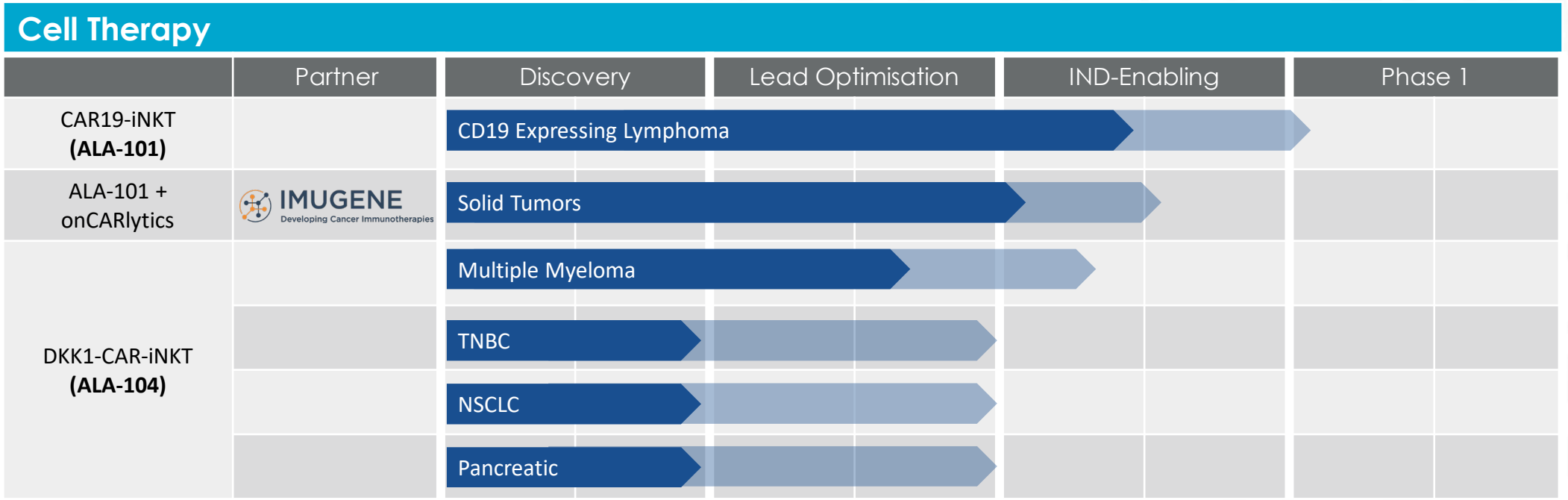
ALA-101 + onCARlytics

ALA-104



Non-Hodgkin's Lymphoma	Head and Neck Cancer	Prostate Cancer	Brain Metastases	Triple Negative Breast Cancer	Pancreatic Cancer	Lung Cancer	Multiple Myeloma

Arovella's Key Milestones Over 18 Months



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
  - Complete studies to assess the novel cytokine technology with the iNKT cell platform

arovella THERAPEUTICS

Arovella Has a Strong Leadership Team

LEADERSHIP

Dr. Michael Baker
CEO & MANAGING DIRECTOR

Dr. Nicole van der Weerden
CHIEF OPERATING OFFICER

Dr. Mini Bharathan
SENIOR VP DEVELOPMENT & TRANSLATIONAL MEDICINE

Dr. Sandhya Buchanan
MANUFACTURING & QUALITY

Ana Radeljevic
BUSINESS DEVELOPMENT

BOARD OF DIRECTORS

Dr. Elizabeth Stoner
BOARD CHAIR

Dr. Debora Barton
DIRECTOR

Mr. Gary Phillips
DIRECTOR

Mr. David Simmonds
DIRECTOR

SCIENTIFIC ADVISORS

Prof. Tassos Karadimitris
Imperial College London

Dr John Maher
CSO Leucid Bio

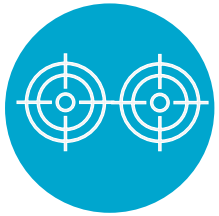
Dr Reuben Benjamin
Kings College London

Professor Qing Yi
Houston Methodist

arovella THERAPEUTICS

Summary – Arovella's CAR-iNKT Cell Platform

A novel allogeneic CAR-iNKT cell platform
iNKT cells serve as an excellent platform to develop allogeneic cell therapies to treat cancer



CAR-iNKT cells have multiple anticancer properties
CAR-iNKT cells are dual-targeting with enhanced cancer killing ability

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

Arovella has an expanding pipeline
ALA-101 and ALA-104 both have the potential to be used to treat haematological malignancies and solid tumors

Arovella has world class partners
Arovella's technologies are licensed from **Imperial College London** and **MD Anderson Cancer Center.** Arovella has an ongoing collaboration with **Imugene**

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

arovella THERAPEUTICS

Thank You

Dr. Michael Baker
CEO & Managing Director

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

arovella
THERAPEUTICS