ASX Release

03 July 2024

INVESTOR PRESENTATION

MELBOURNE, AUSTRALIA 3 July 2024: Arovella Therapeutics Ltd (ASX: ALA), a biotechnology company focused on developing its invariant Natural Killer T (iNKT) cell therapy platform, is pleased to provide an update to investors in the form of the attached presentation.

The presentation will be used in Arovella's non-deal investor roadshow being conducted this week.

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.

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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'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 glycolipid 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. Arovella is also expanding into solid tumour treatment through its CLDN18.2-targeting technology licensed from Sparx Group. Arovella will also incorporate its IL-12-TM technology into its solid tumour programs.

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.

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.

ASX:**ALA**

arovella THERAPEUTICS

Non-deal roadshow

July

2024

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Arovella's strengths

Off-the-Shelf iNKT Cell Platform

Developing off-the-shelf iNKT cell therapies to target blood cancers and solid tumour cancers

Lead Product Advancing to Clinic

ALA-101, potential treatment for CD19-expressing blood cancers, progressing to Phase 1 clinical trials, expected to commence in 2024

Addressing Key Unmet Need

Our iNKT cell platform is well positioned to solve key challenges that hamper the cell therapy sector

Strong Leadership Group

Leadership team and Board have proven experience in drug development, particularly cell therapies

Strategic Acquisitions

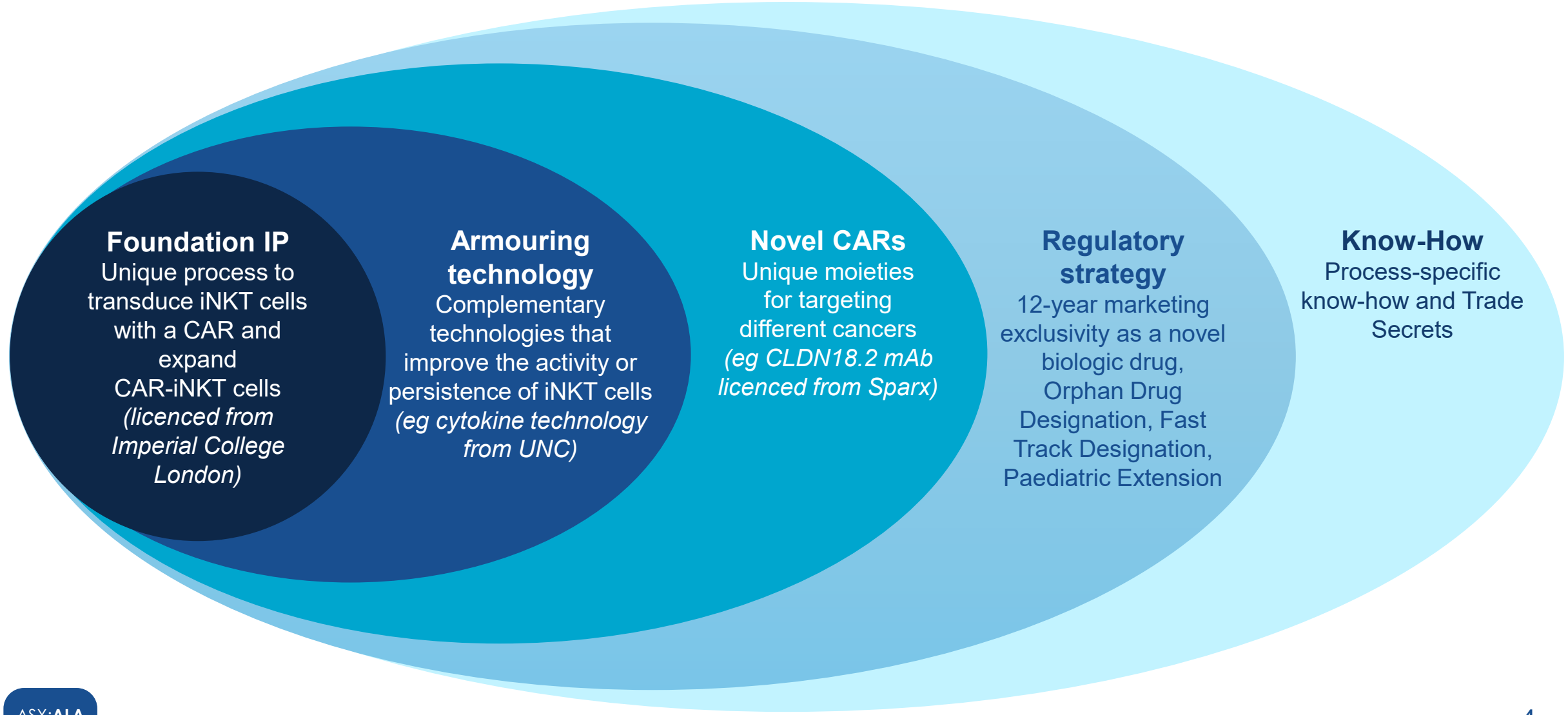
Focused on acquiring innovative technologies that strengthen its cell therapy platform and align with its focus areas

Unique Value Proposition

Arovella is among few companies globally developing an iNKT cell therapy platform

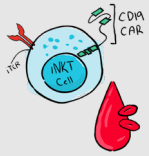
Arovella's iNKT cell strategy

Incorporating world class IP to target a range of tumour types



Arovella's path to patient

Taking Arovella's first CAR-iNKT therapeutic to human trials in FY2025

PRODUCT	TECHNOLOGY ACQUISITION	PRE-CLINICAL CONFIRMATION	LENTIVIRUS MANUFACTURING	MANUFACTURING PLATFORM	FDA (IND) / TGA (CTA)	PHASE 1 CLINICAL TRIAL	PHASE 2 CLINICAL TRIAL
CD19-iNKT Blood Cancer 	✓	✓	✓	✓		FY2025	
CLDN18.2-iNKT Gastric Cancer 	✓			✓			
CAR-iNKT Other Cancers 				✓			

- IL-12-TM will be incorporated into Arovella's solid tumour programs
- Armouring using IL-12-TM can be incorporated using the same manufacturing platform

***Abbreviations**: FDA, U.S. Food and Drug Administration; IND, Investigational New Drug Application; TGA, Therapeutic Goods Administration; CTA, Clinical Trials Approval*

Financial overview

Financial Snapshot

ASX CODE	ALA
Market capitalisation[1]	$147.1 million
Shares on issue	1,050.2 million
52-week low / high[1]	$0.042 / $0.185
Cash Balance (Mar 31, 2024)[2]	$15.31 million

Major Shareholders

Shareholder	Ownership (%) [1]
RICHARD JOHN MANN	64,458,288 (6.16%)
MERCHANT FUNDS MANAGEMENT	62,996,544 (6.02%)
MB INVESTMENT CAPITAL PTY LTD	27,636,115 (2.64%)
UBS NOMINEES PTY LTD	25,620,196 (2.45%)
MR JAMES EVAN HUGHES-MORRIS	21,917,196 (2.10%)

1. *As of 21 June 2024*
2. *Includes the proceeds of the Placement announced 26 March 2024*

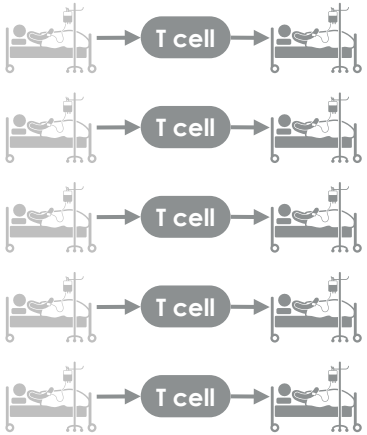
Recent cell therapy transactions[1]

Date	Type of deal	Acquirer/Licensee	Target/Licensor	Cell Type	Stage	Upfront (US$M)	Milestones (US$M)	Total deal value (US$M)
May-24	Research collaboration	Xyphos	Poseida Therapeutics	T cell	TBD	$50	$550	$600
Dec-23	Acquisition	AstraZeneca	Gracell	T Cell	Phase 1b	$1,000	$200	$1,200
Nov-23	Collaboration and investment[2]	AstraZeneca	cellectis	Not specified	Platform	$25	$70-220 per product	
Aug-23	Licence[3]	Imugene Developing Cancer Immunotherapies	Precision Biosciences	T Cell	Phase 1b	$21	$206	$227
Aug-23	Strategic investment (ROFR) [4]	astellas	Poseida Therapeutics	T Cell	Phase 1	$25	$0	$25
May-23	Licence	janssen	CBMG Cellular Biomedicine Group	T Cell	Phase 1b	$245	*undisclosed*	
Jan-23	Acquisition	AstraZeneca	neogene Therapeutics	T Cell	Phase 1	$200	$120	$320
Oct-22	Development collaboration[5]	Gilead	Arcellx	T Cell	Phase 2	$225	*undisclosed*	
Sep-22	Research collaboration	Genentech A Member of the Roche Group	ArsenalBio	T Cell	Preclinical	$70	*undisclosed*	
Aug-22	Licence & strategic collaboration	Roche	Poseida Therapeutics	T Cell	Phase 1	$110	$110	$220
Sep-21	Development collaboration	Genentech A Member of the Roche Group	Adaptimmune	T Cell	Preclinical	$150	$150	$300
Aug-21	Research collaboration	Gilead	APPIA BIO	iNKT Cell	Preclinical	*undisclosed*	*undisclosed*	$875
May-21	Acquisition	Athenex	kuur Therapeutics	iNKT Cell	Phase 1	$70	$115	$185
Jun-21	Acquisition	eterna	Novellus Therapeutics	Multiple	Preclinical	$125	$0	$125

1. See the last slide for deal references; 2. Cellectis will receive a US$220m equity investment from Astra Zeneca plus tiered royalties. Milestones are payable for 10 products; 3. Precision is eligible for double digit royalties on net sales and $145 million in milestone payments and tiered royalties for additional programs; 4. Poseida also received a US$25m equity investment from Astellas; 5. Arcellx also received a US$100m equity investment from Gilead

Current CAR-T technology challenges

One CAR-T product **only** treats the patient who supplied the T cells



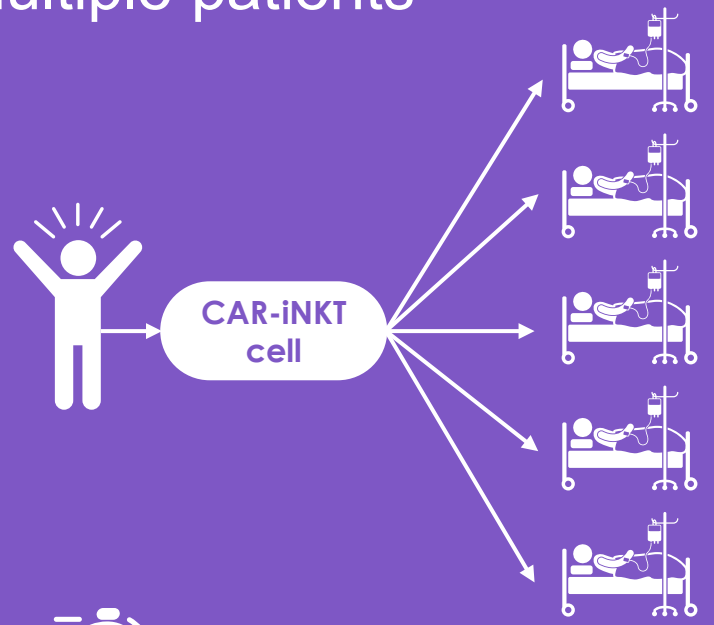
Each manufacturing batch is **patient-specific**

Patient must wait **3-4 weeks** for therapy

- Manufacturing & supply chain **costs are high**
- T cells **can be compromised** due to disease
- **Limited centres** can collect and manufacture
- **Time is an issue** for patients with aggressive disease
- Manufacturing run **failures can occur**

ALA's solution:

One CAR-iNKT batch from **a healthy donor** treats multiple patients

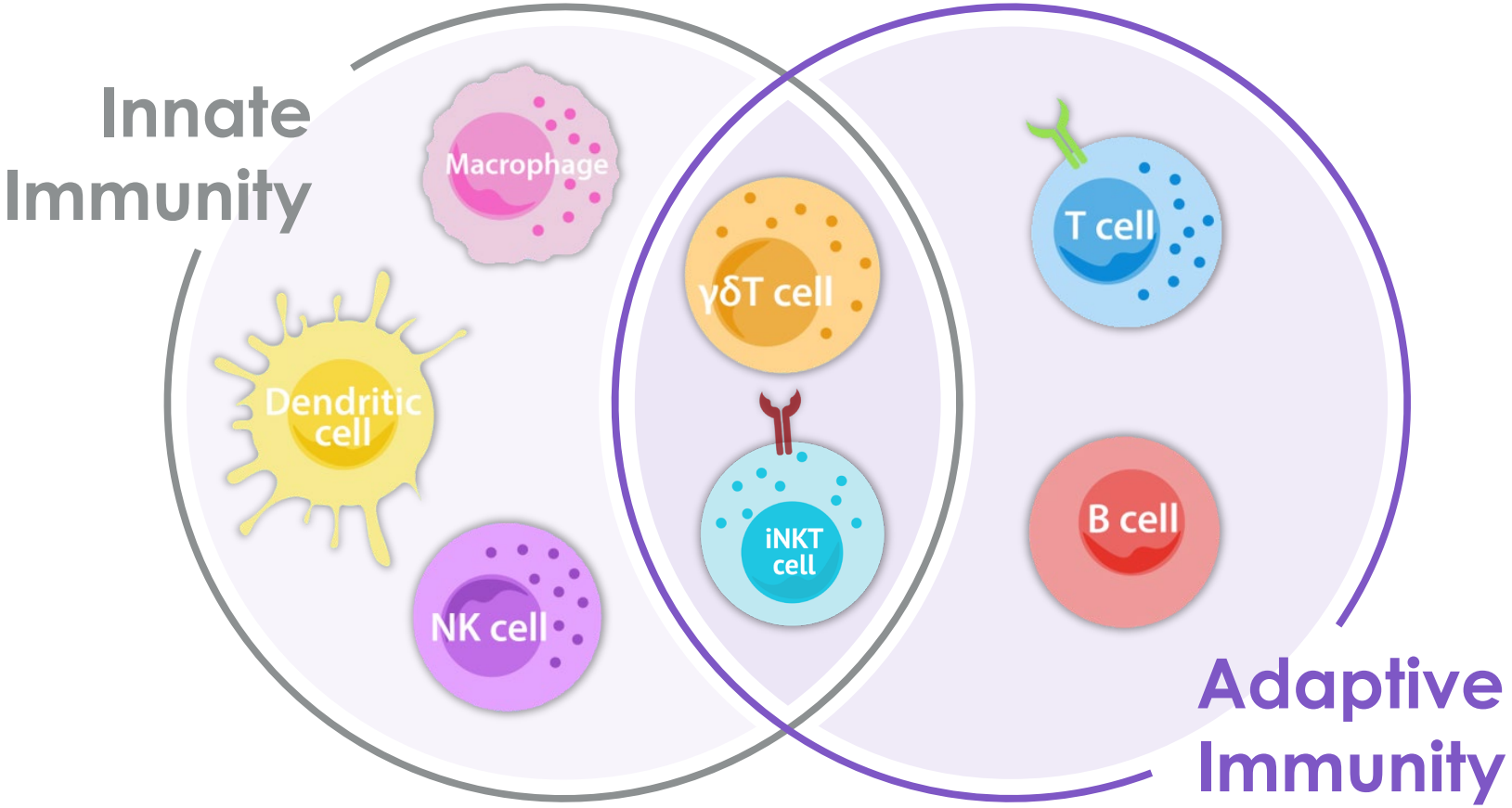


1 week

Patients ready to dose within 1 week

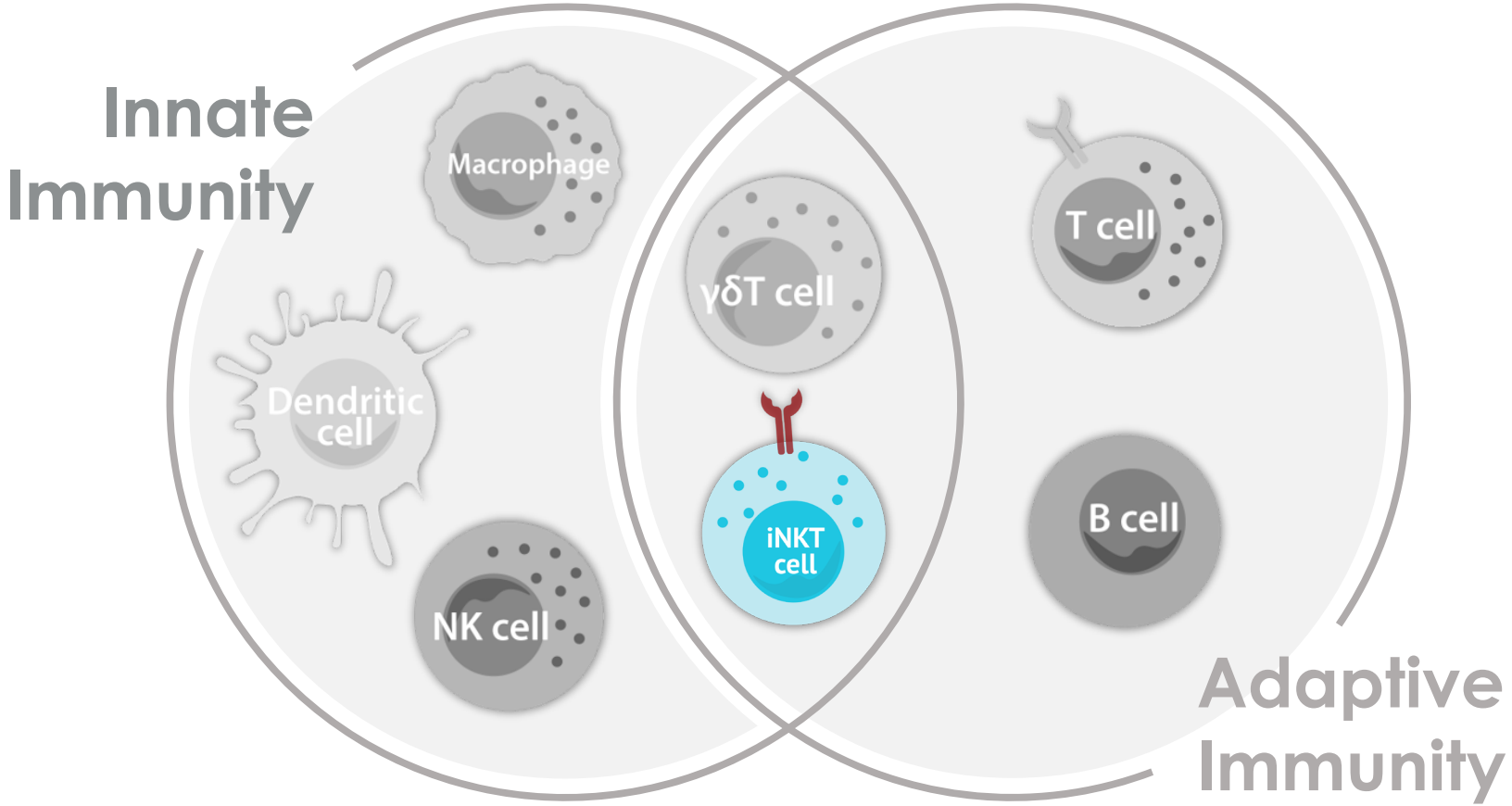
Introducing invariant Natural Killer T (iNKT) cells

Bridging the innate and adaptive immune system



iNKT cells represent a next-generation cell therapy

Innate properties make them ideal for use in cell therapy



Strong safety profile

- Don't cause graft versus host disease (GvHD)

Front line of the human immune system

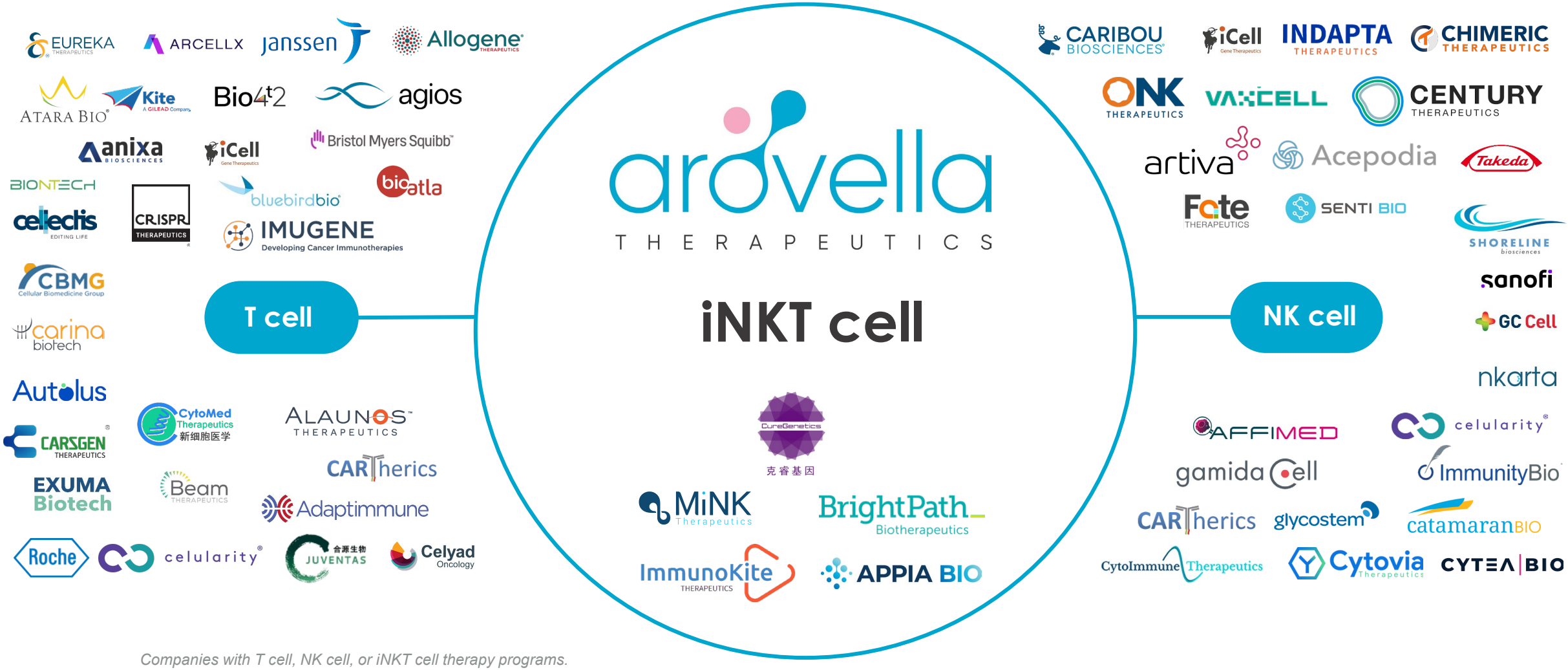
- Bridge innate & adaptive immune responses
- Contain both T cell & NK cell killing mechanisms
- Naturally target & kill cancers that express CD1d

Multiple anti-cancer properties

- Shape the tumour microenvironment by blocking/killing pro tumour cells (TAMs/MDSCs)
- Infiltrate tumours & secrete signaling molecules to activate other immune cells to kill tumour cells

A differentiated position

T cell and NK cell sectors are competitive, iNKT cells remain untapped

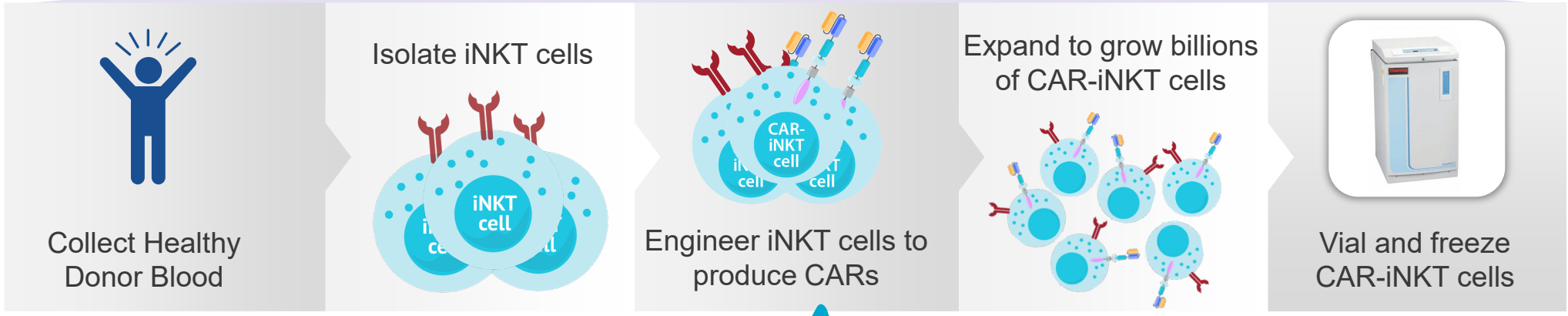


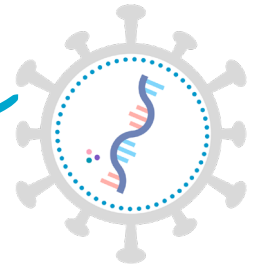
Companies with T cell, NK cell, or iNKT cell therapy programs.
Source: Company analysis based on public information

Clinic-ready manufacturing process developed

Semi-automated process suitable for large-scale and late-phase clinical development

TECHNOLOGY ACQUISITION → PRE-CLINICAL CONFIRMATION → LENTIVIRUS MANUFACTURING → **MANUFACTURING PLATFORM** → FDA (IND) / TGA (CTA) → PHASE 1 CLINICAL TRIAL → PHASE 2 CLINICAL TRIAL





Lentivirus for any CAR

Completed GMP manufacture of ALA-101 lentivirus

Completed process development with excellent results:

- **High yield**, >5,000-fold expansion of CAR-iNKT cells
- **>60% of the cells have the CAR (i.e. CAR-iNKT cells)**
- **>99% purity** of iNKT cells
- **Semi-automated**, suitable for **large-scale production**
- Potential to leverage **FDA Platform Designation**

Taking ALA-101 into first-in-human trials

ALA is progressing towards its ALA-101-001 phase 1 study

Clinical trial design and KOL engagement

Engagement with key opinion leaders and potential sites and preparation of protocol synopsis

GMP manufacturing of clinical drug product

ALA is finalizing key GMP inputs and conducting process qualification in preparation for clinical manufacture

IND-enabling studies and regulatory submission

ALA is conducting IND-enabling non-clinical safety and efficacy studies to support regulatory approval

Selection of sites and CRO

ALA will select participating sites and a clinical research organisation partner who will manage the study

Regulatory approval and site startup

Once regulatory approval is obtained, sites will be activated and screening of patients can commence

ALA-101-001: Phase 1 first-in-human study

Dose escalation and dose expansion study in patients with CD19+ blood cancers

Patients with relapsed or refractory CD19+ non-Hodgkin's lymphoma (NHL, including DLBCL, FL, MCL, MZL) and CD19+ leukemias (including B-ALL, CLL and HCL).

- Single dose of ALA-101 following lymphodepletion regimen
- **Primary objectives**
  - To evaluate the safety and tolerability of ALA-101 in adult patients with CD19+ NHL or leukemia
- **Secondary objectives**
  - To determine the most appropriate dose of ALA-101 for Phase 2 clinical trials for adult patients with CD19+ NHL or leukemia
  - To evaluate the preliminary efficacy of ALA-101
  - To characterise the pharmacokinetic (PK) profile of ALA-101

Part 1: Dose Escalation

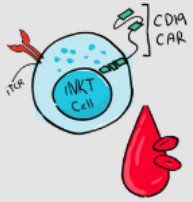
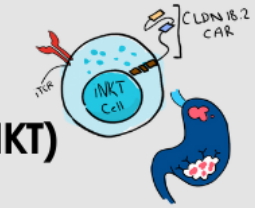
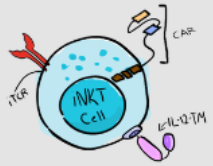
- 4 dose levels
- ~9-12 patients
- CD19+ NHL and leukemias

Part 2 (Phase 1b): Dose Expansion

- Dose level selected from Part 1
- ~20 patients
- Sub-indications selected from Part 1

Abbreviations: *NHL, non-Hodgkin's lymphoma; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; B-ALL, B-cell acute lymphoblastic leukemia; CLL, chronic lymphocytic leukemia; HCL, hairy cell leukemia*

Arovella's expanding pipeline

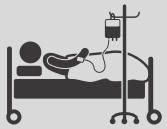
PRODUCT	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1
ALA-101 (CAR19-iNKT) 	CD19 Expressing cancers	CD19 Expressing Lymphoma		
ALA-105 (CLDN18.2-iNKT) 	CLDN18.2 positive solid tumours	Gastric & Pancreatic Cancers		
IL-12-TM 	Solid Tumours	Solid Tumours		

Upcoming milestones for FY2025

July **2024**

July **2025**

ALA-101 (CD19)	▪ Complete cGMP manufacture for Phase 1 clinical trials ▪ Complete preparatory activities for Phase 1 study, preparation of regulatory dossier, engagement with clinical sites and KOLs ▪ Commence phase 1 dose escalation study for ALA-101 in patients with CD19+ NHL and leukemia
ALA-105 (CLDN18.2)	▪ Proof-of-concept testing for CLDN18.2-iNKT cells and optimisation of the CAR construct for robust efficacy ▪ Generate animal data for CLDN18.2 targeting CAR-iNKT cells against gastric cancer and/or pancreatic cancer ▪ Commence activities to manufacture ALA-105 for clinic (e.g. lentiviral vector)
IL-12-TM Integration	▪ Integrate IL-12-TM into solid tumour programs and test its efficacy in anti-tumour models ▪ Enter into a Sponsored Research Agreement (SRA) with Professor Gianpietro Dotti's research group
Pipeline expansion	▪ Continue to identify and acquire novel technologies that enhance and expand Arovella's iNKT cell therapy platform



Arovella is funded to dose patients with ALA-101 during FY2025

Abbreviations: *cGMP, current good manufacturing practice; KOLs, key opinion leaders; NHL, non-Hodgkin's lymphoma*

Summary

Novel allogeneic CAR-iNKT cell platform

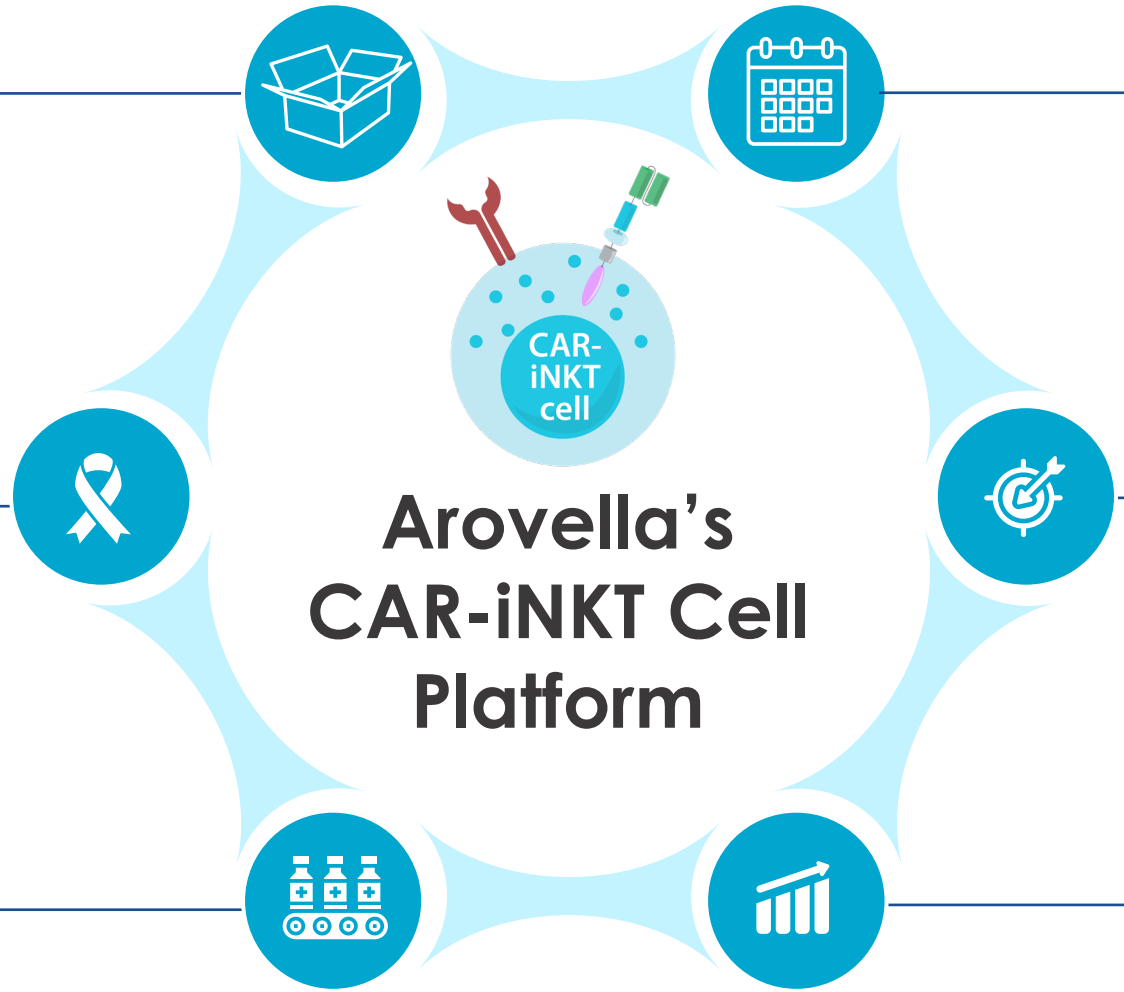
iNKT cells serve as an excellent platform to develop allogeneic, or “off-the-shelf”, cell therapies to treat cancer

Improved manufacturing logistics

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

CAR-iNKT cells have multiple anticancer properties

CAR-iNKT cells have multiple anti-cancer properties that may support enhanced efficacy over other immune cell types



Lead product progressing to clinical trials

ALA-101, a potential treatment for CD19-expressing blood cancers, is being progressed to Phase 1 clinical trials, expected to commence in 2025

Arovella has an expanding pipeline

Arovella continues to expand the iNKT cell platform and can add different CARs, leveraging its manufacturing process

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

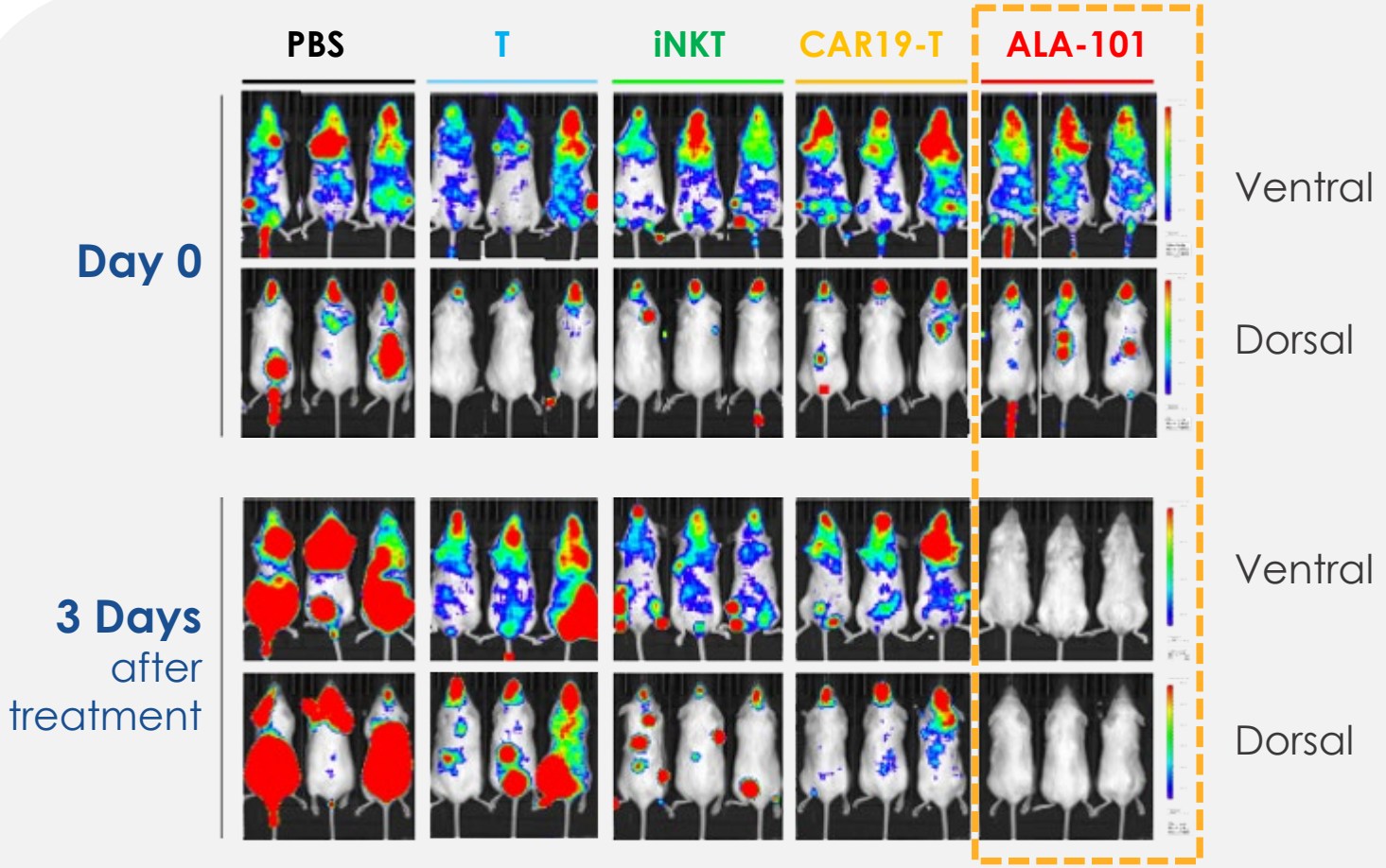
ALA-101 (CAR19-iNKT cells)

A next generation **off-the-shelf** cell therapy for CD19 expressing cancers

ALA-101: enhanced tumour killing *in vivo*

ALA-101 rapidly eradicates tumour cells in mice

- 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 (CAR19-iNKT cells)
- After three days, ALA-101 resulted in significant regression of tumour cells
- In all other treatments, there was strong tumour cell persistence
- ALA-101 displays swift action

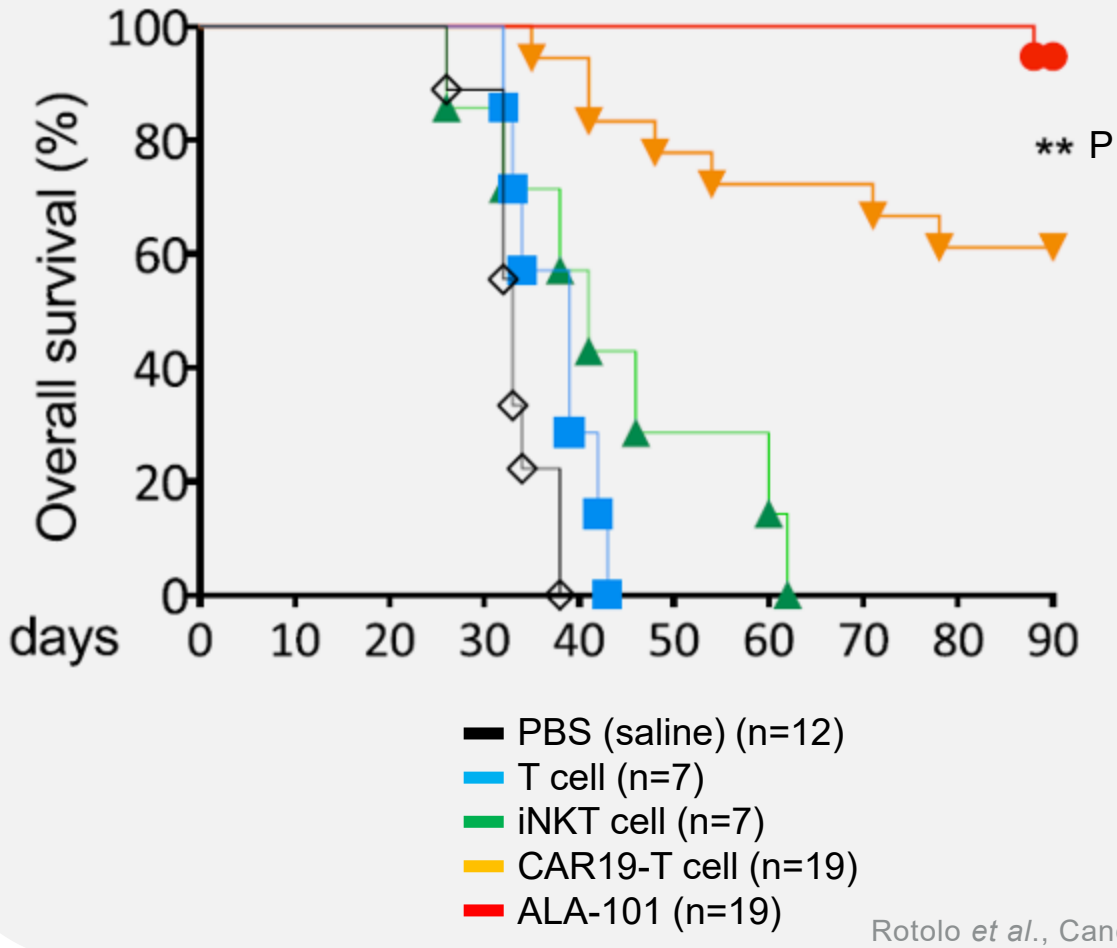


Rotolo *et al.*, Cancer Cell (2018)

ALA-101: next generation cell therapy

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 (CAR19-iNKT cells)
- 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

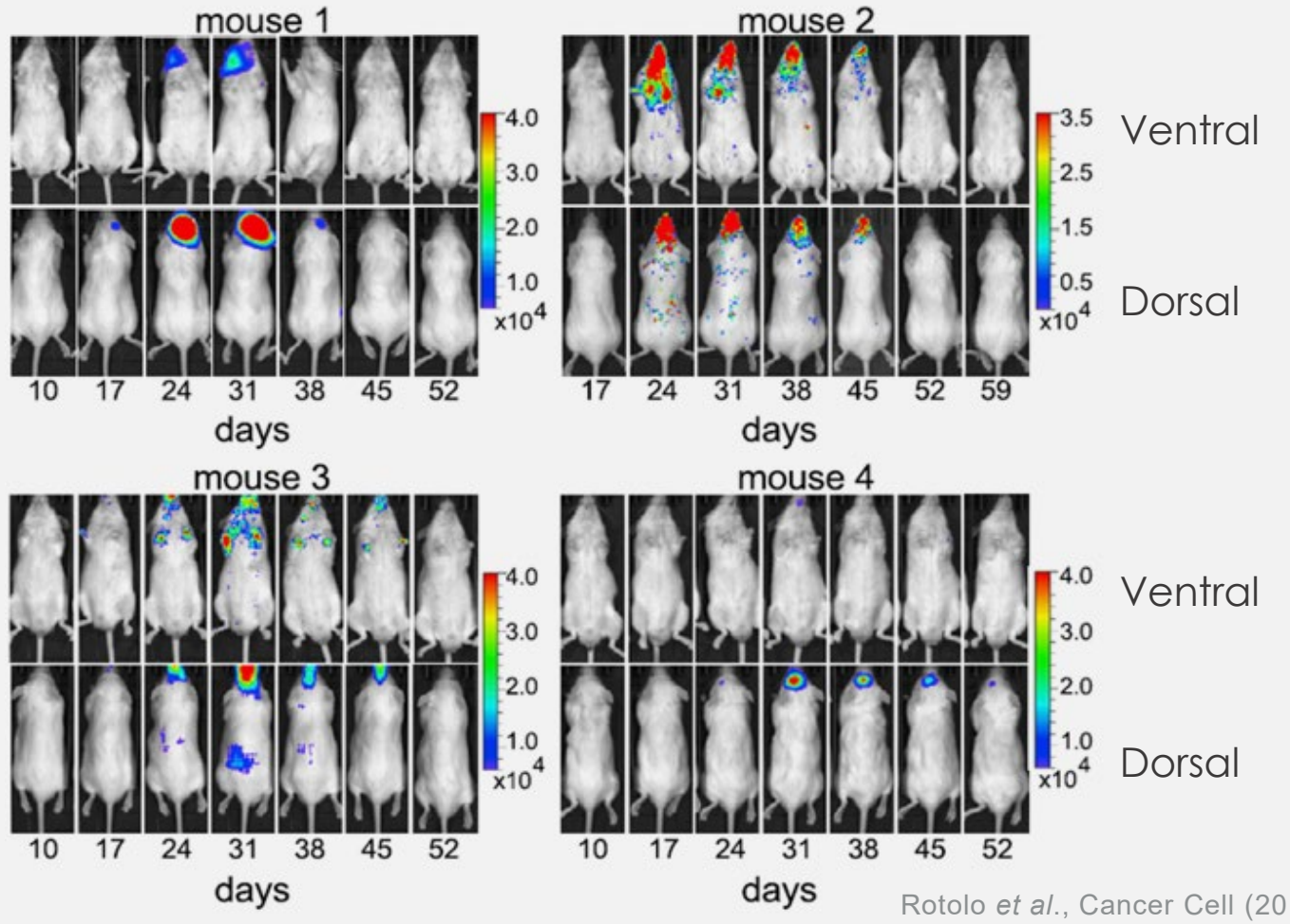


Rotolo *et al.*, Cancer Cell (2018)

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 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)

iNKT cells to target solid tumours

Arovella is implementing its strategy to target and kill solid tumours – 90% of newly diagnosed cancer cases[1]

1. *https://www.cancer.gov/types/common-cancers*

Arovella's strategies to combat solid tumours

Arovella is using three approaches to expand the iNKT cell platform into solid tumours

License novel cancer targets

Identify and license new targets that are expressed in multiple cancers to incorporate into Arovella's iNKT cell therapy platform

Armour iNKT cells

Enhance the performance of iNKT cells by equipping iNKT cells with novel armouring technologies

Create unique partnerships

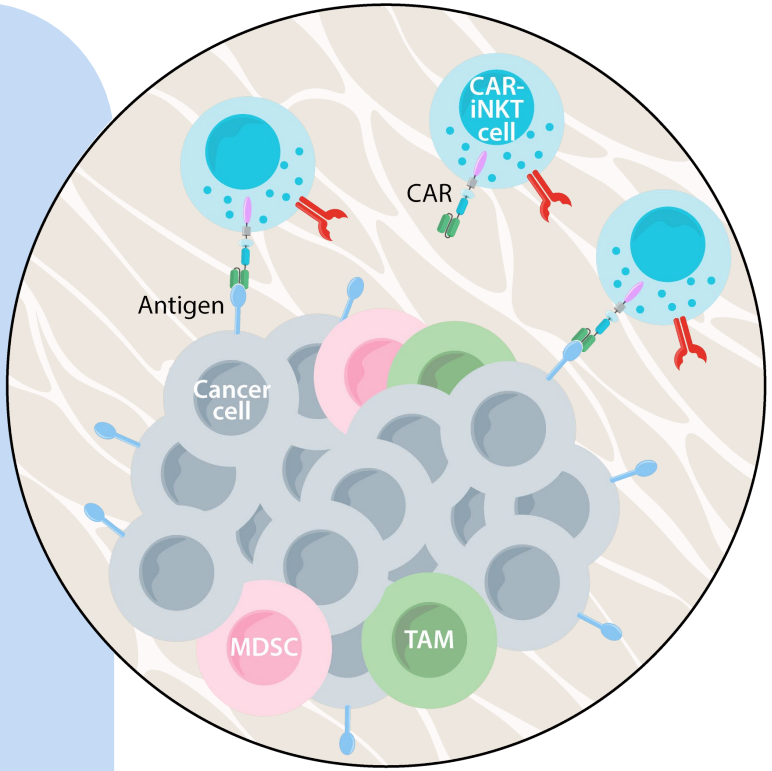
Create partnerships to use novel combination therapies with synergistic effects

Solid tumours pose challenges to cell therapies

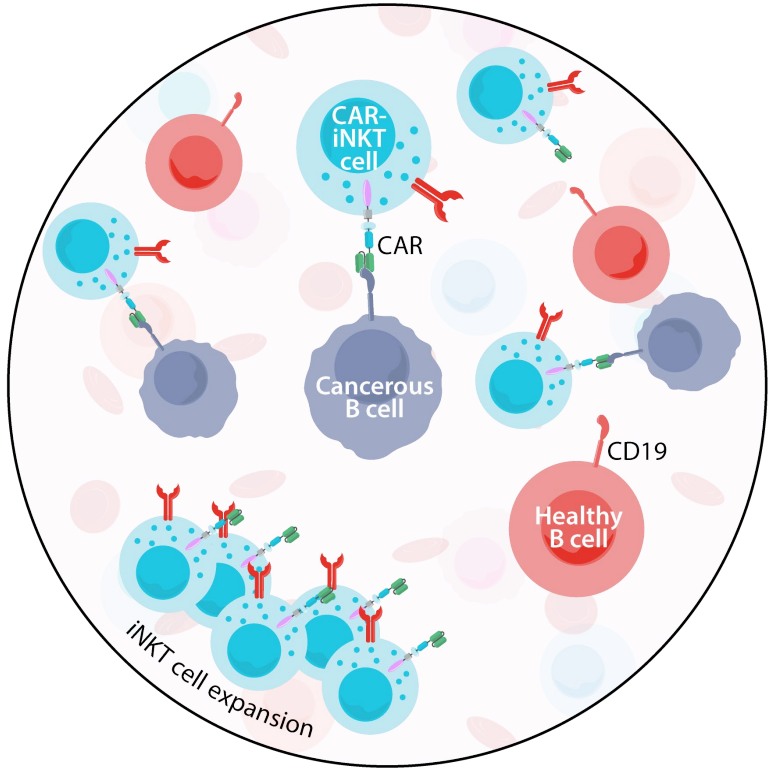
Solid tumours are more

difficult to treat with cell therapies

- Access to tumour
- Lack of antigen specificity and uniformity
- Tumour microenvironment contains cells that support cancer cell growth



Solid tumour



Blood cancer

iNKT cells:

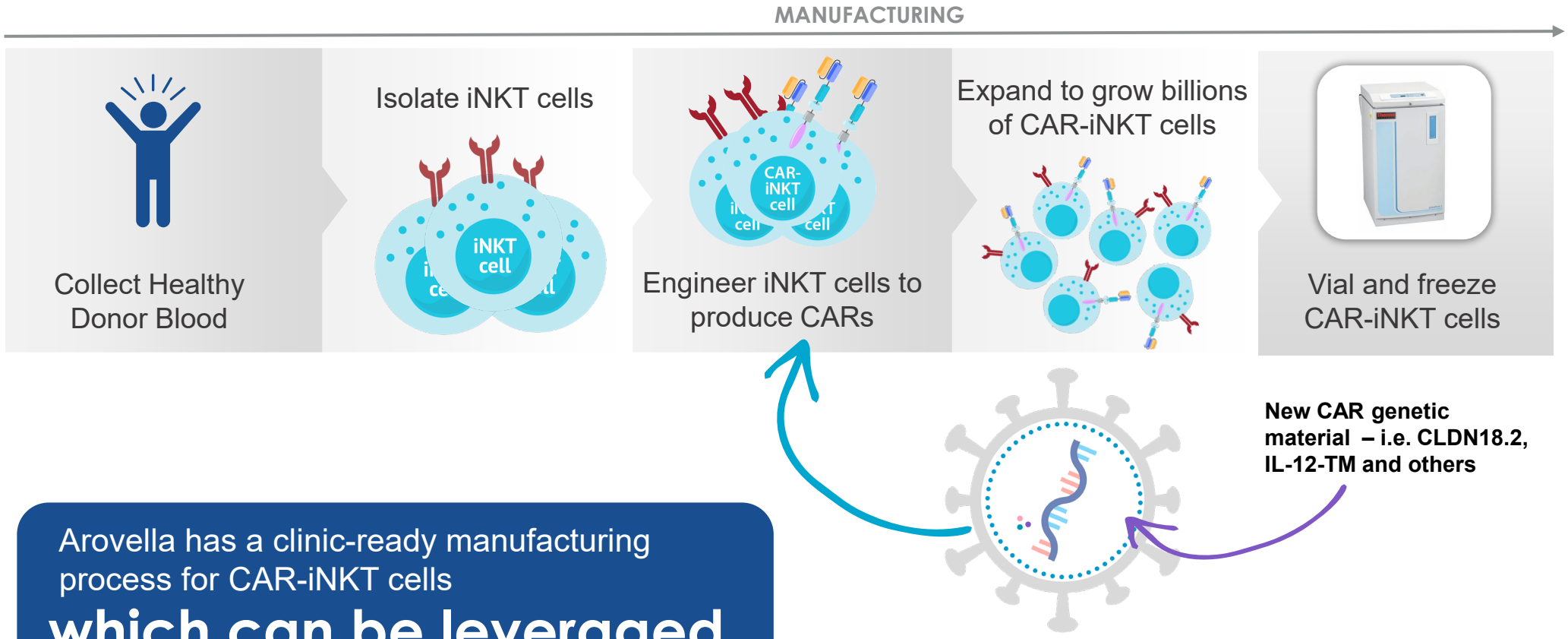
- Home to tissues and infiltrate tumours
- Modify the TME to block or kill cells that promote tumour growth and recruit helpful immune cells

Abbreviations: *TAM, Tumour Associated Macrophage; MDSC, Myeloid Derived Suppressor Cell; CAR, Chimeric Antigen Receptor*

Add additional CARs for novel targets

New CARs

Arovella's manufacturing process can be leveraged for multiple cancer types



Arovella has a clinic-ready manufacturing process for CAR-iNKT cells

which can be leveraged to create many CAR-iNKT cell products to target multiple cancer types

New lentivirus generated for each new CAR

ALA-105 (CLDN18.2-iNKT cells)

A next generation **off-the-shelf** cell therapy for CLDN18.2+ solid tumours

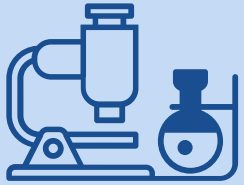
Claudin 18.2 (CLDN18.2)

A promising solid tumour target

CLDN18.2 overexpression has been

identified in several types of cancers

- gastric cancer **(GC)**
- gastroesophageal junction cancer **(GEJC)**
- pancreatic cancer **(PC)**
- esophageal cancer **(EC)**
- ovarian adenocarcinoma **(OAC)**
- lung cancers **(LC)**



Validated target

with first CLDN18.2-targeting monoclonal antibody **approved in Japan in March 2024**

Gastric cancer

market alone expected to reach **$10.7 billion** by 2031[1]

1. https://www.alliedmarketresearch.com/gastric-cancer-market-A74458#:~:text=The%20global%20gastric%20cancer%20market,cells%20lining%20of%20the%20stomach

iNKT cell armouring (IL-12-TM)

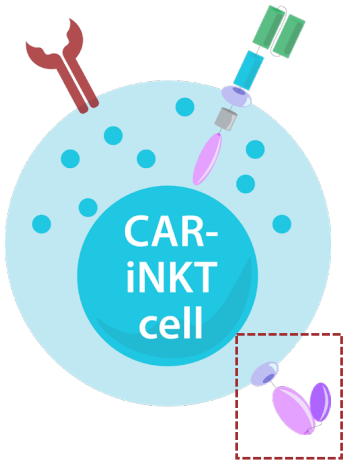
Armouring strategy to enhance activity of CAR-iNKT cells against solid tumours

“Armouring” CAR-iNKT cells

Armouring

IL-12-TM (cytokine technology) enhances CAR-iNKT cell activity in solid tumours

IL-12-TM



IL-12-TM

IL-12-TM is a modified version of IL-12

with a membrane anchor that links it to the surface of CAR-iNKT cells. By linking it to the surface of iNKT cells, it can enhance CAR-iNKT cells without being released into the blood stream, making it safer.

The IL-12-TM is incorporated into the lentiviral vector and system and **does not require changes to the manufacturing process**

iNKT cells + IL-12-TM

Expand more and survive for longer
than CAR-iNKT cells lacking the cytokine

10x more circulating CAR-iNKT cells
4 weeks after treatment in a mouse model

Superior anti-tumour activity
compared to CAR-iNKT cells lacking the cytokine

The technology has been published in the prestigious, peer reviewed journal **Nature Communications**

nature › nature communications › articles › article

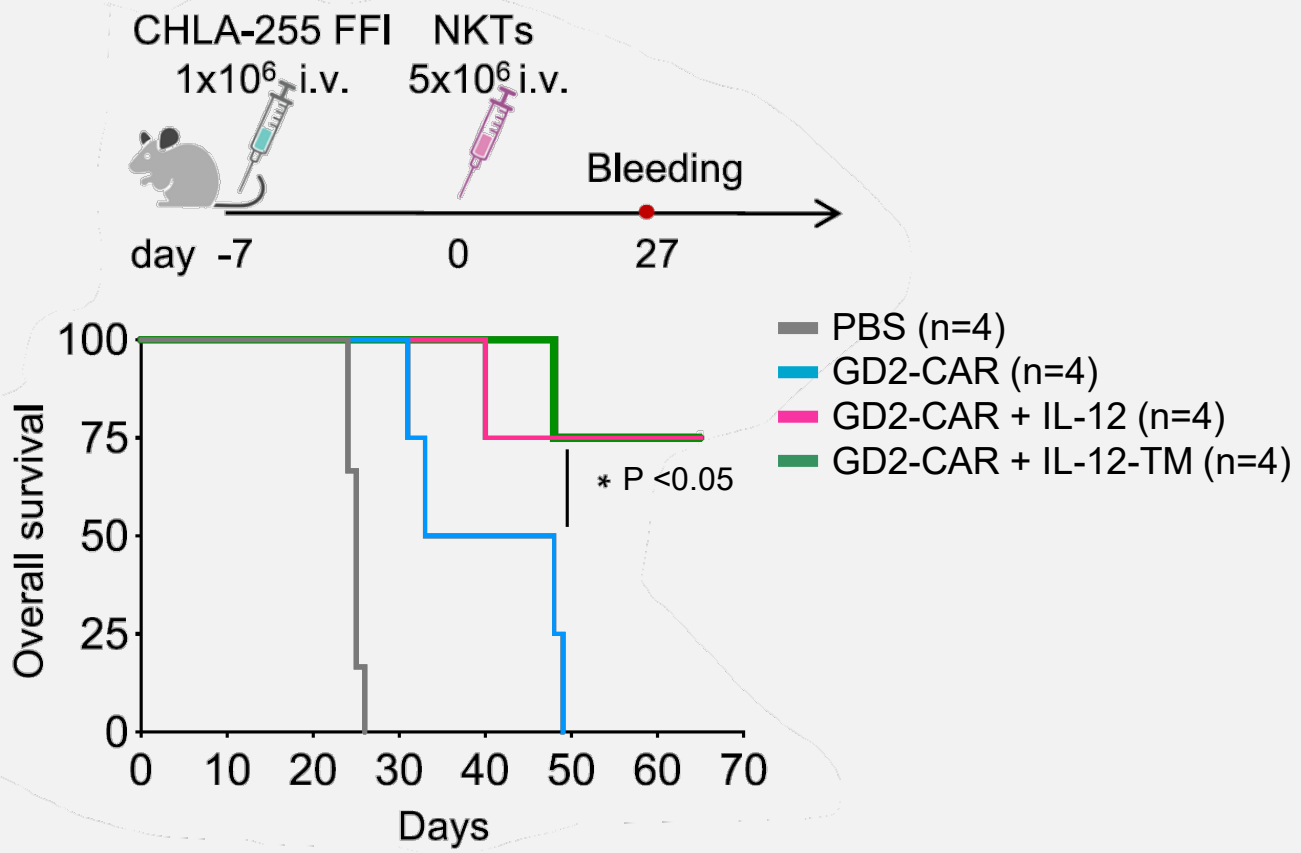
Article | Open access | Published: 02 January 2024

IL-12 reprograms CAR-expressing natural killer T cells to long-lived Th1-polarized cells with potent antitumor activity

Key benefits of IL-12-TM for CAR-iNKT cells

IL-12-TM enhances antitumor activity of CAR-iNKT cells

- Tumour cells expressing GD2 and were intravenously delivered into mice before treatment with CAR-iNKT cells
- Mice were treated with:
  - PBS (saline)
  - GD2-CAR
  - GD2-CAR + IL-12
  - GD2-CAR + IL-12-TM
- After 60 days, only mice treated with GD2-CAR + IL-12 or IL-12-TM remained alive
- IL-12-TM enhances CAR-iNKT cell numbers and antitumour activity



Landoni *et al.*, Nature Communications (2024)

Key benefits of IL-12-TM for CAR-iNKT cells

We expect IL-12-TM to enhance Arovella's CAR-iNKT cell platform

Increases CAR-iNKT cell numbers

IL-12-TM prolongs persistence of CAR-iNKT cells. Cells continue to proliferate and increase in number.

IL-12-TM is not released from CAR-iNKT cells

IL-12-TM is not released from CAR-iNKT cells and is expected to be safer than secreted IL-12.

Enhances CAR-iNKT cell antitumour activity

IL-12-TM enhances CAR-iNKT antitumor activity against solid tumour cancers such as neuroblastoma.

ASX:**ALA**

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THERAPEUTICS

Thank You

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