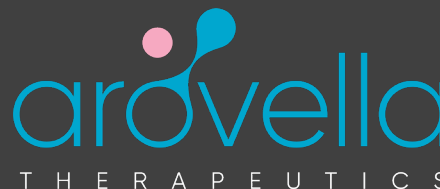


ASX: ALA

Arovella Therapeutics Limited
ACN 090 987 250



ASX Release

2 July 2025

INVESTOR PRESENTATION

MELBOURNE, AUSTRALIA 2 JULY 2025: Arovella Therapeutics Ltd (ASX: ALA) is pleased to provide an update to investors in the form of the attached presentation.

This presentation will be used at Arovella's non-deal roadshow being conducted this week.

Release authorised by the Managing Director and Chief Executive Officer at Arovella Therapeutics Pty Ltd.

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 into solid tumour treatment through its CLDN18.2-targeting technology licensed from Sparx Group. Additional tumour targeting technologies are anticipated to be used in conjunction with Arovella's 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; **α GalCer** – alpha-galactosylceramide is a specific ligand for human and mouse natural killer T cells. It is a synthetic glycolipid.

ASX: ALA

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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



Non-deal roadshow

July

2025



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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

Addressing Key Unmet Need

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

Strategic Acquisitions

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

Strong Leadership Group

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

Clinic-ready Manufacturing Process

Arovella has successfully developed a proprietary clinic-ready manufacturing process to produce CAR-iNKT cells

Lead Product Advancing to Clinic

ALA-101, potential treatment for CD19-positive blood cancers, progressing to phase 1 clinical trials, expected to commence in early 2026



Arovella's strong leadership group

Leadership



Dr Nicole van der Weerden
CHIEF OPERATING OFFICER



Dr Robson Dossa
HEAD MANUFACTURING & QUALITY



Dr Michelle Ferguson
HEAD RESEARCH & DEVELOPMENT



Jacqueline Cumming
SNR DIRECTOR CLINICAL DEVELOPMENT

Board of Directors



Dr Elizabeth Stoner
INTERIM CHAIR



Dr Michael Baker
CEO & MANAGING DIRECTOR

































Dr Debora Barton
DIRECTOR



Mr Gary Phillips
DIRECTOR

Recent cell therapy transactions¹

Date	Type of deal	Acquirer/Licensee	Target/Licensors	Cell Type	Stage	Upfront (US\$M)	Milestones (US\$M)	Total deal value (US\$M)
Jun-25	Acquisition			In vivo CAR	Phase 1	\$2,100	\$0	Up to \$2,100
Mar-25	Acquisition			In vivo CAR	Phase 1	\$425	\$575	\$1,000
Nov-24	Acquisition			Allo T cell	Phase 1	~\$1,038	~\$462	\$1,500
May-24	Research collaboration			T cell	TBD	\$50	\$550	\$600
Dec-23	Acquisition			T Cell	Phase 1b	\$1,000	\$200	\$1,200
Nov-23	Collaboration and investment ²			Not specified	Platform	\$25	\$70-220 per product	
Aug-23	Licence ³			T Cell	Phase 1b	\$21	\$206	\$227
Aug-23	Strategic investment (ROFR) ⁴			T Cell	Phase 1	\$25	\$0	\$25
May-23	Licence			T Cell	Phase 1b	\$245	undisclosed	
Jan-23	Acquisition			T Cell	Phase 1	\$200	\$120	\$320
Oct-22	Development collaboration ⁵			T Cell	Phase 2	\$225	undisclosed	
Aug-22	Licence & strategic collaboration			T Cell	Phase 1	\$110	\$110	\$220
Sep-21	Development collaboration			T Cell	Preclinical	\$150	\$150	\$300
Aug-21	Research collaboration			iNKT Cell	Preclinical	undisclosed	undisclosed	\$875
May-21	Acquisition			iNKT Cell	Phase 1	\$70	\$115	\$185

1. See the last slide for deal references; 2. Celectis 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

Financial overview

Financial Snapshot

ASX CODE	ALA
Market capitalisation ¹	\$130.2 million
Shares on issue	1,183.9 million
52-week low / high	\$0.068 / \$0.210
Cash Balance (31 Mar, 2025)	\$23.5 million

Major Shareholders

Shareholder	Ownership (%) ²
BIOTECH CAPITAL MANAGEMENT PTY LTD ³	108,526,184 (9.17%)
RICHARD JOHN MANN ³	67,487,674 (5.70%)
NETWEALTH INVESTMENTS LIMITED ³	47,072,126 (3.98%)
UBS NOMINEES PTY LTD	29,930,527 (2.53%)
BLACKBURNE CAPITAL PTY LTD	23,008,988 (1.94%)

1. As of 27 June 2025
2. As of 21 March 2025
3. Holding includes associated entities and parties

ALA Price and Volume - 12 Months¹



Highlights for CY 2025 to date...



Cash and cash equivalents
at 31 March, 2025 of

**\$23.5
million**



Completed \$15 million placement to fully fund enrolment and report initial safety and efficacy data for the phase 1 trial for ALA-101



Successfully transferred the ALA-101 manufacturing process into cGMP environment in readiness for clinical batches



Held the first meeting of the recently formed clinical advisory board



Entered into sponsored research agreement with University of North Carolina to advance solid tumour and IL-12-TM armouring programs



Generated functional Claudin 18.2-targeting chimeric antigen receptor



Signed an exclusive Option for two new CARs targeting neuroblastoma and hepatocellular carcinoma



Targeting cancer using cell therapies

Cell Therapy has revolutionised blood cancer treatment

CAR-T cells have demonstrated their curative potential in blood cancers



The Cell Therapy market
is expected to reach
\$61.2 billion
by 2030¹

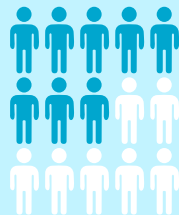


Cure

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



Strong Sales



40-60%

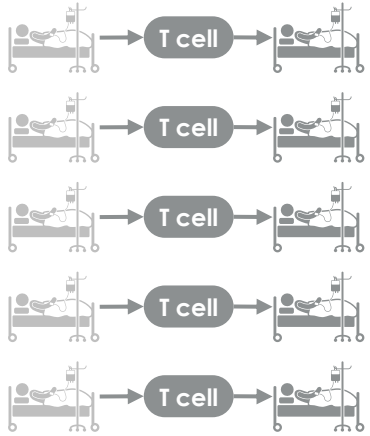
Patients relapse
post-CAR-T therapy²

Product	Approval Year	2024 Revenue
 YESCARTA[®] (axicabtagene ciloleucel) <small>Suspension for IV infusion</small>	2017	US\$1570m ³
 KYMRIAH[®] (tisagenlecleucel) <small>Suspension for IV infusion</small>	2017	US\$442m ⁴
 Abecma[®] (idecabtagene vicleucel) <small>Suspension for IV infusion</small>	2021	US\$242m ⁵

1. <https://www.businesswire.com/news/home/20230529005130/en/Global-Cell-Therapy-Market-Report-2023-Advancements-in-Biotechnology-Drives-Growth---ResearchAndMarkets.com>
2. Zinzi et al., 2023 Pharmacological Research - 10.1016/j.phrs.2023.106742
3. <https://www.gilead.com/news/news-details/2025/gilead-sciences-announces-fourth-quarter-and-full-year-2024-financial-results>.
4. https://www.novartis.com/sites/novartis_com/files/2025-01-interim-financial-report-en.pdf
5. <https://ir.2seventybio.com/news-releases/news-release-details/2seventy-bio-reports-preliminary-full-year-us-abecma-sales-and>

Current CAR-T technology challenges

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



Each manufacturing batch is **patient-specific**

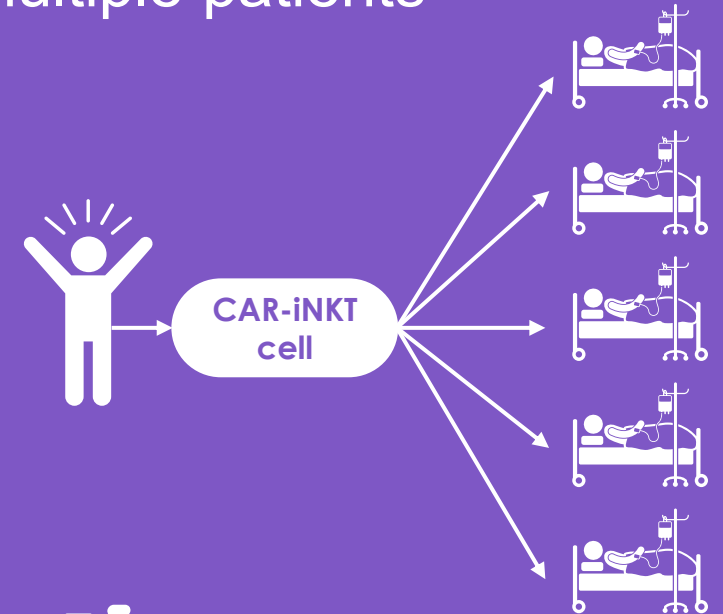
Patient must wait **3-4 weeks** for therapy



- ❗ 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

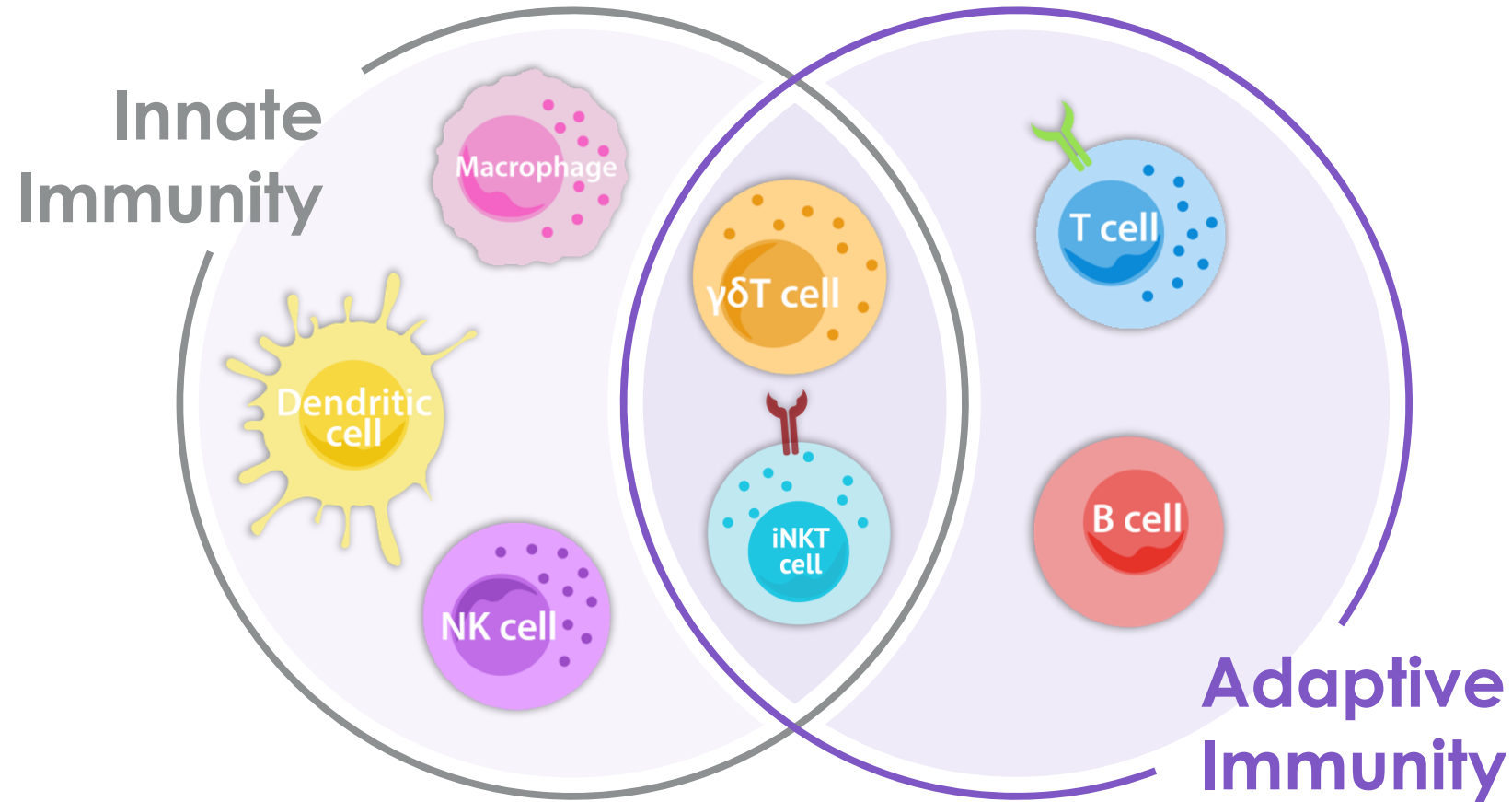


 **1 week**

Patients ready to dose within 1 week

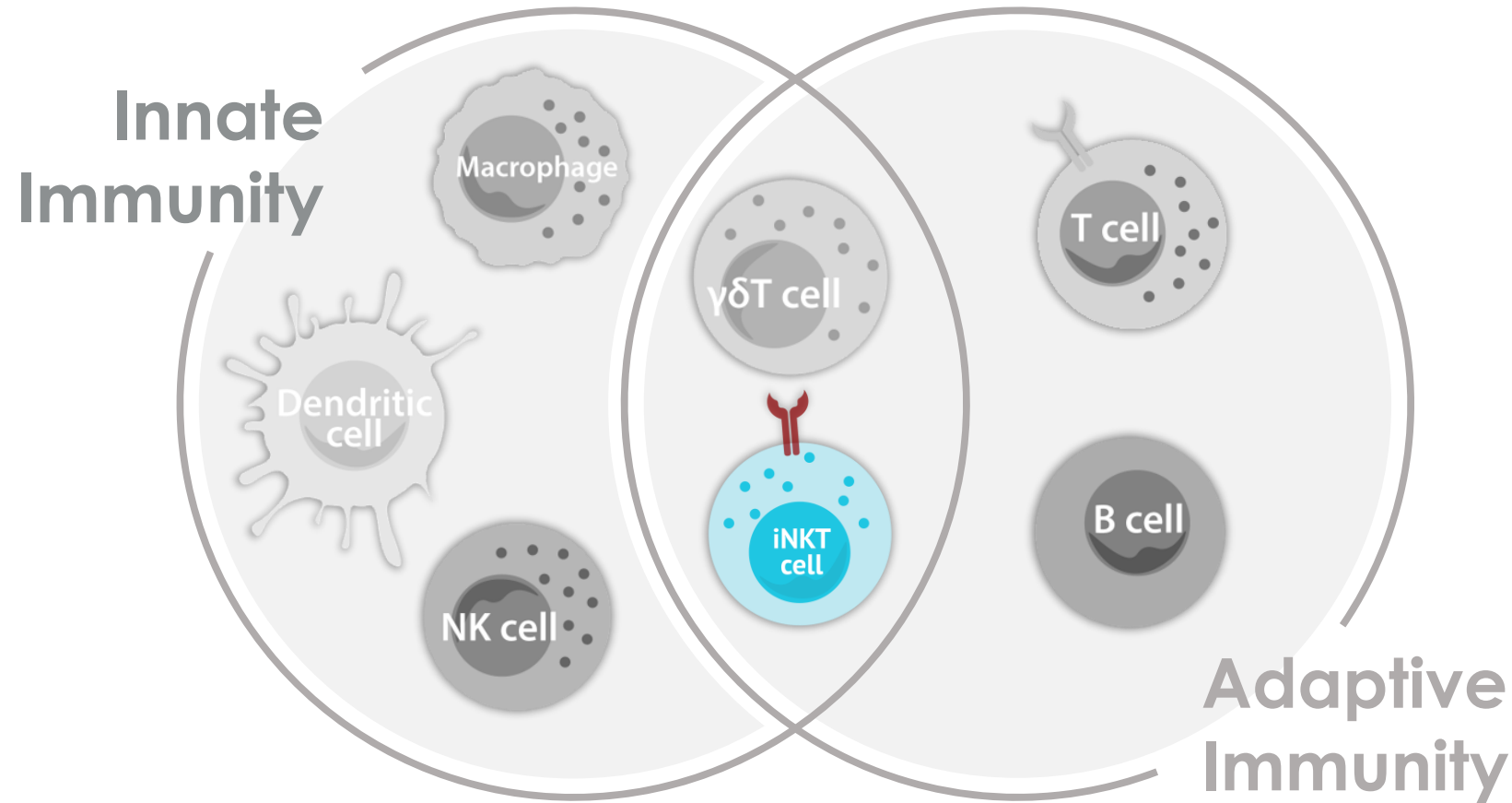
Introducing invariant Natural Killer T (iNKT) cells

Bridging the innate and adaptive immune system



iNKT cells represent a next-generation cell therapy

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

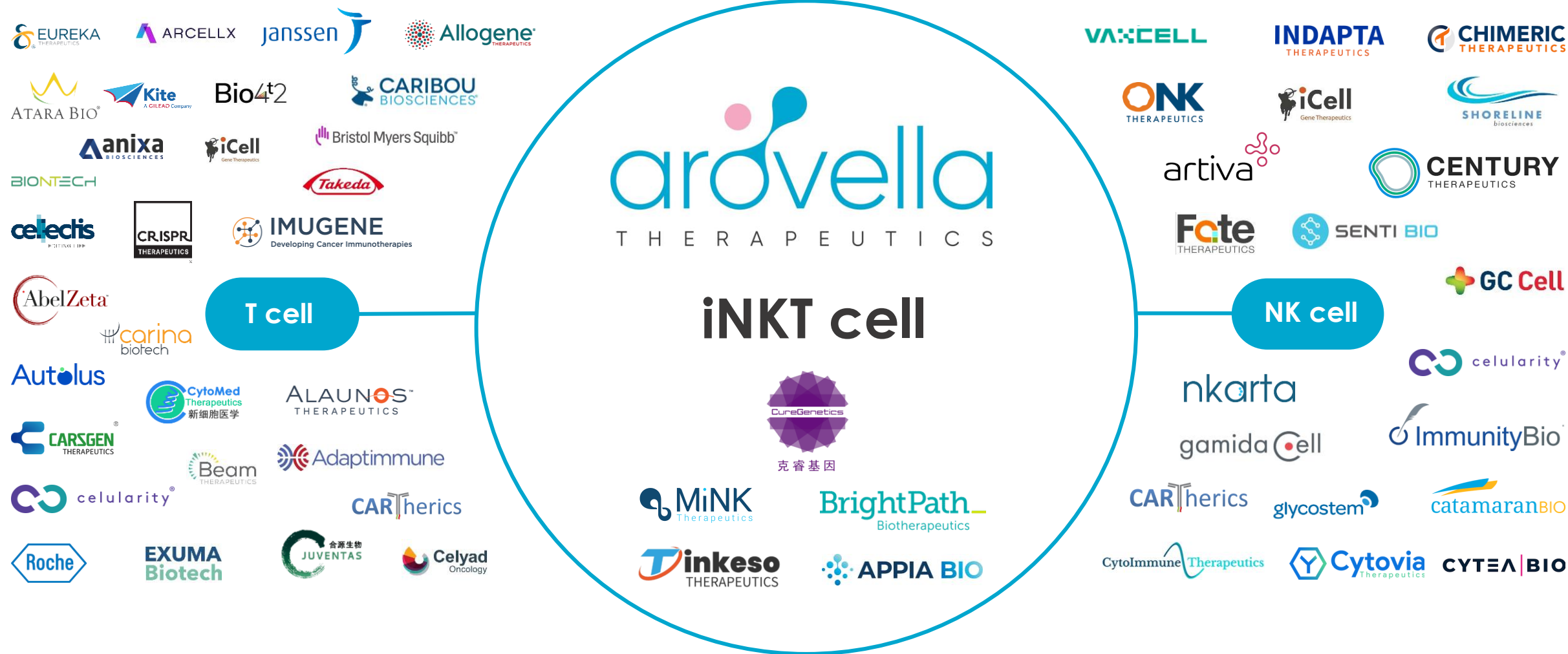
- Bridge innate & adaptive immune responses
- Contain both T cell & NK cell killing mechanisms
- Naturally target & kill cancers that express CD1d

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





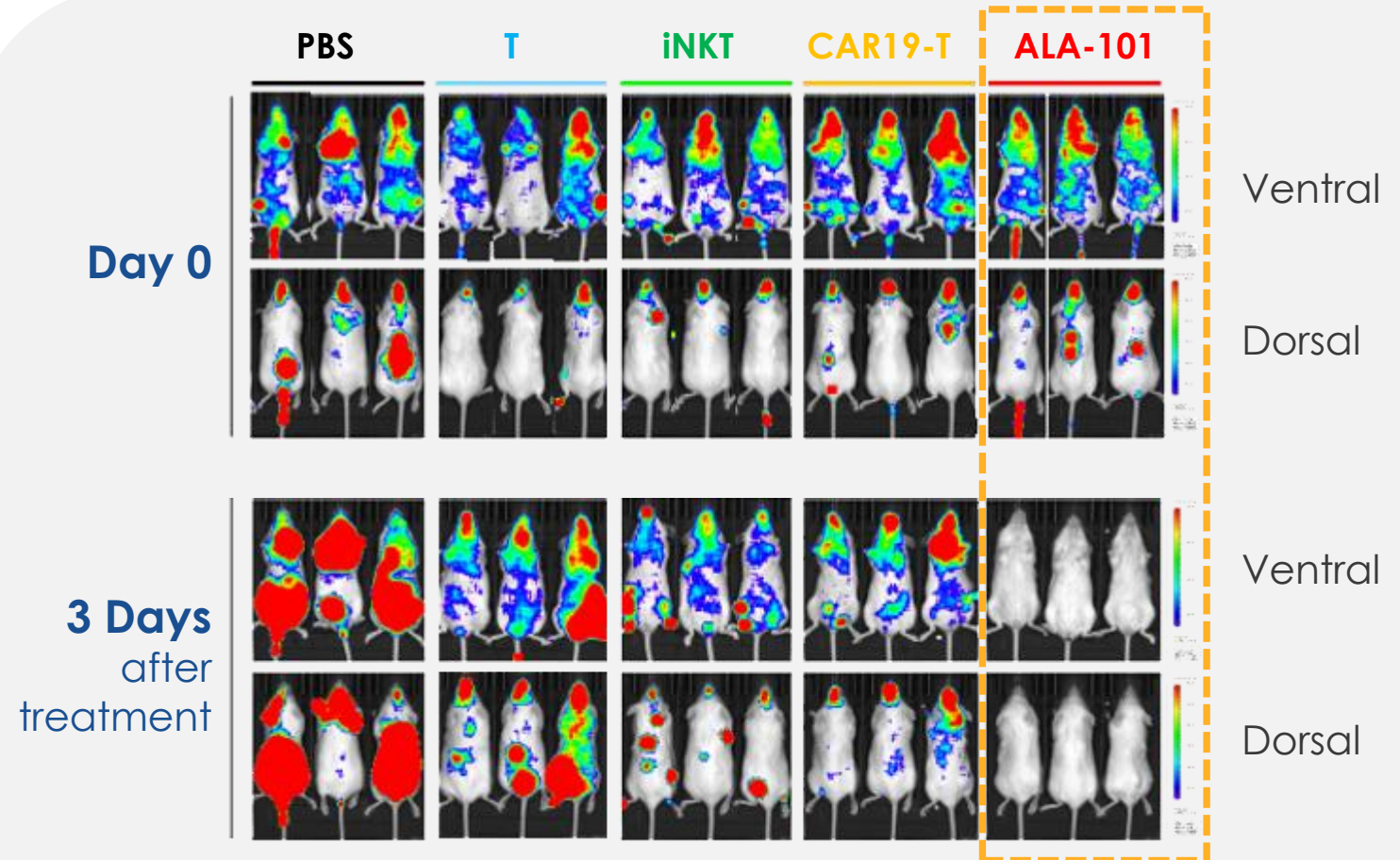
ALA-101 (CAR19-iNKT cells)

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

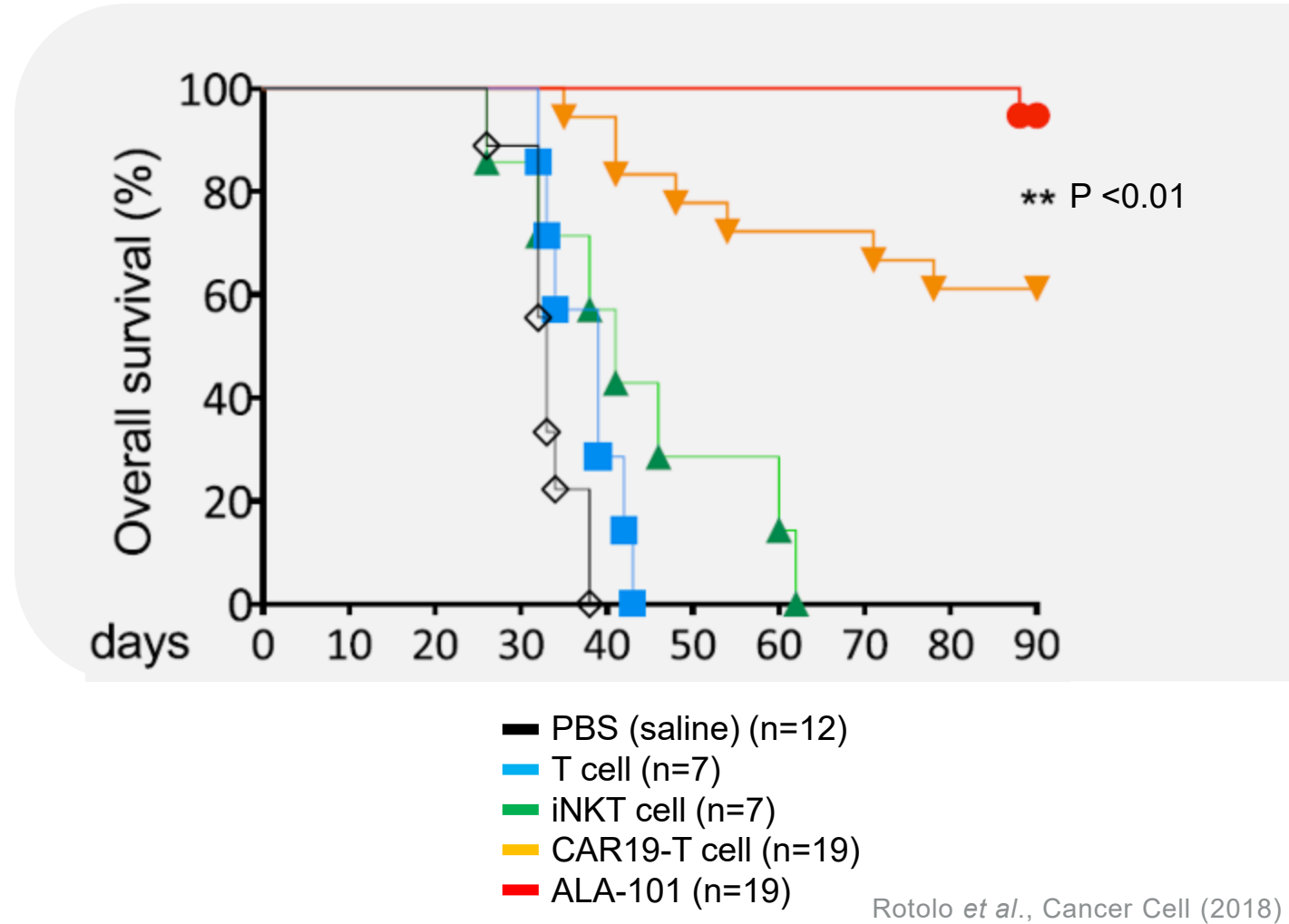


Rotolo *et al.*, Cancer Cell (2018)

ALA-101: next generation cell therapy

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

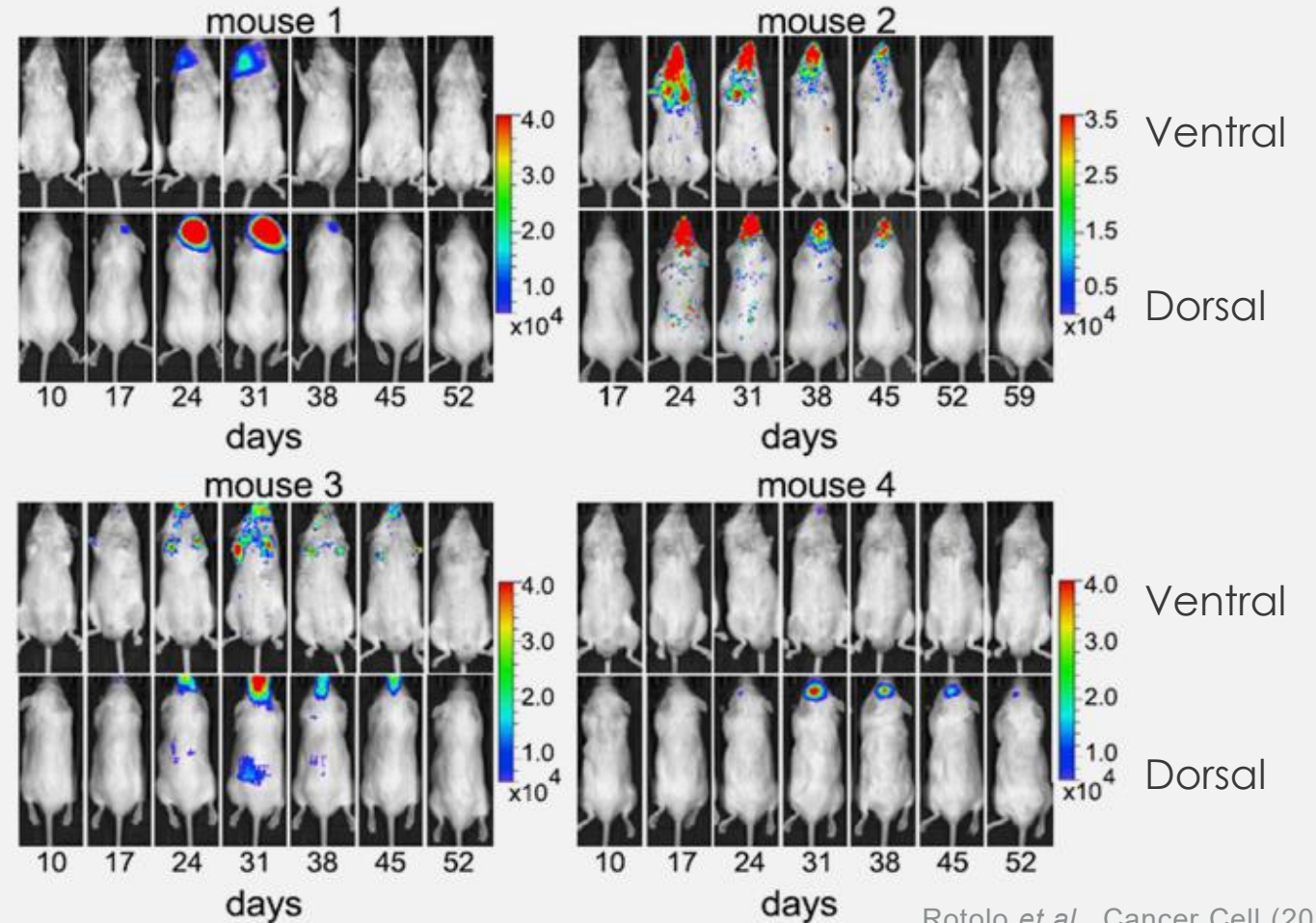
- Tumour cells positive for **CD19** and **CD1d** were intravenously delivered into mice
- Mice were treated with:
 - PBS (saline)
 - Unmodified T cells (T)
 - Unmodified iNKT cells (iNKT)
 - CAR19-T cells
 - ALA-101 (CAR19-iNKT cells)
- After 90 days, only mice treated with CAR19-T cells or ALA-101 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-positive cancers



ALA-101: spontaneous secondary remission

ALA-101 activity may persist to eradicate tumour cells following relapse

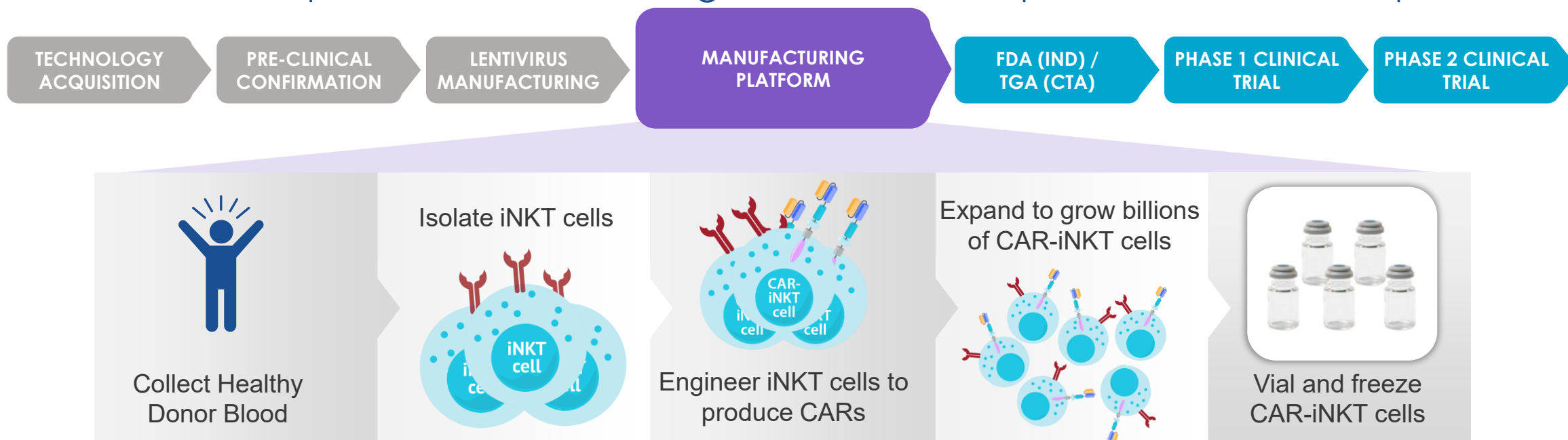
- Four mice treated with ALA-101 had the cancer return to the brain
- In all four mice, the cancer was eliminated a second time with no additional dosing
- This provides evidence that CAR19-iNKT cells can survive and continue to protect against cancer cells in vivo
- Potential to use ALA-101 to treat central nervous system lymphoma or brain metastases



Rotolo et al., Cancer Cell (2018)

Clinic-ready manufacturing process developed

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



Progressed tech transfer to the GMP suites for clinical manufacturing

- **High yield**, >5,000-fold expansion of CAR-iNKT cells
- **>99% purity** of iNKT cells with a **balance of CD4- and CD4+ cells**
- **Semi-automated**, suitable for **large-scale production**
- Runs now being completed in the **GMP suites** using **GMP reagents**
- New knowledge becomes Arovella **trade secret** and **IP**
- New products can be **created plug and play** by substituting the lentivirus



Completed GMP manufacture of ALA-101 lentivirus

Lentivirus for any CAR

Pathway to US FDA IND

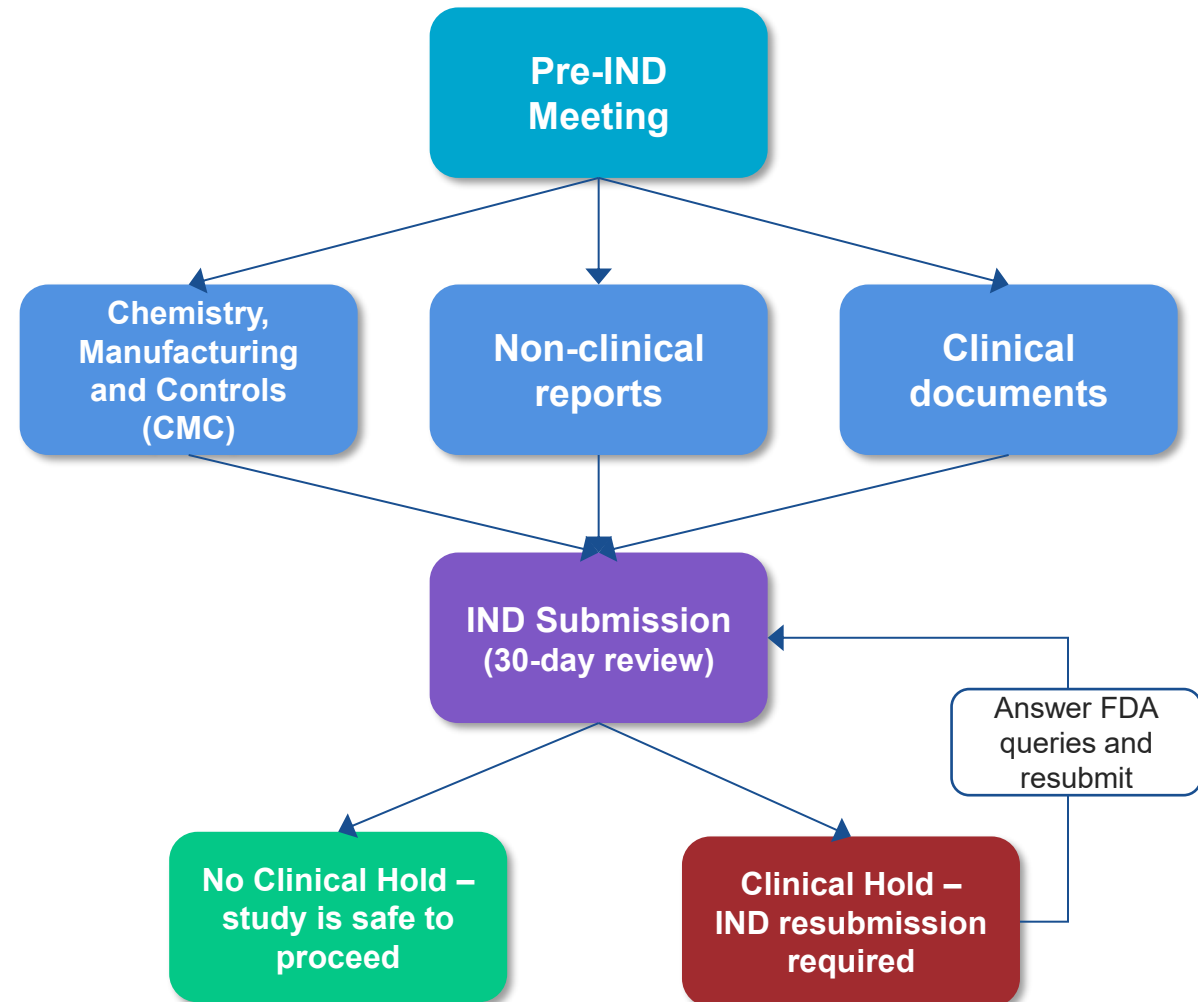
Arovella is working to have the highest chance of a successful IND submission

Early interactions with the FDA to discuss the proposed clinical program

Generation of data for manufacturing and non-clinical studies. Study reports generated and IND is prepared, including clinical documents

Investigational New Drug (IND) application submitted to the FDA

FDA outcome is reached, and the study is approved, or the IND receives a clinical hold



Positioning the ALA-101 IND for success

IND filing is delayed to maximise the chance of acceptance



Chemistry Manufacturing and controls (CMC)

- **Process development** - complete
- **Tech transfer to cGMP suites** - complete
- **Analytical method development** - ongoing

Development of assays requested by FDA during pre-IND meeting took longer than anticipated

- **Release of key GMP reagents** - ongoing

Arovella is considering additional consultation with the FDA prior to IND submission to align on testing requirements for a key reagent not incorporated in the final product

- **Clinical batches manufactured**



Non-Clinical

- **In vivo efficacy** - complete
- **In vitro safety** - complete*
- **In vitro efficacy** - complete*

**Note Arovella intends to complete in vitro safety and efficacy studies on future ALA-101 clinical batches*



Clinical

- **CRO selection** - ongoing
- **Protocol development** - ongoing
- **Site selection** - ongoing
- **HREC submission** - post IND acceptance
- **Site start-up**

- Drafting of the IND submission documents is well underway
- We anticipate the IND will be submitted and accepted in CY2025

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 total
- CD19+ lymphoma

Part 2 (phase 1b): Dose Expansion

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

iNKT cells to target solid tumours

Arovella is implementing its strategy to target and kill solid tumours – 90% of newly diagnosed cancer cases¹

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

iNKT cells have features that may make them useful for treating solid tumours



Solid tumours are more
**difficult
to treat
with cell
therapies**



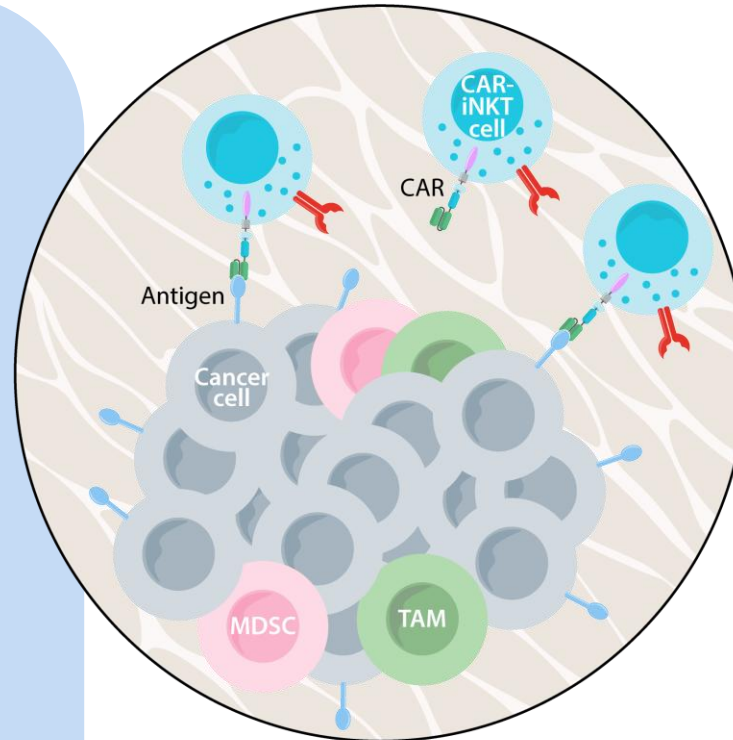
Access to tumour



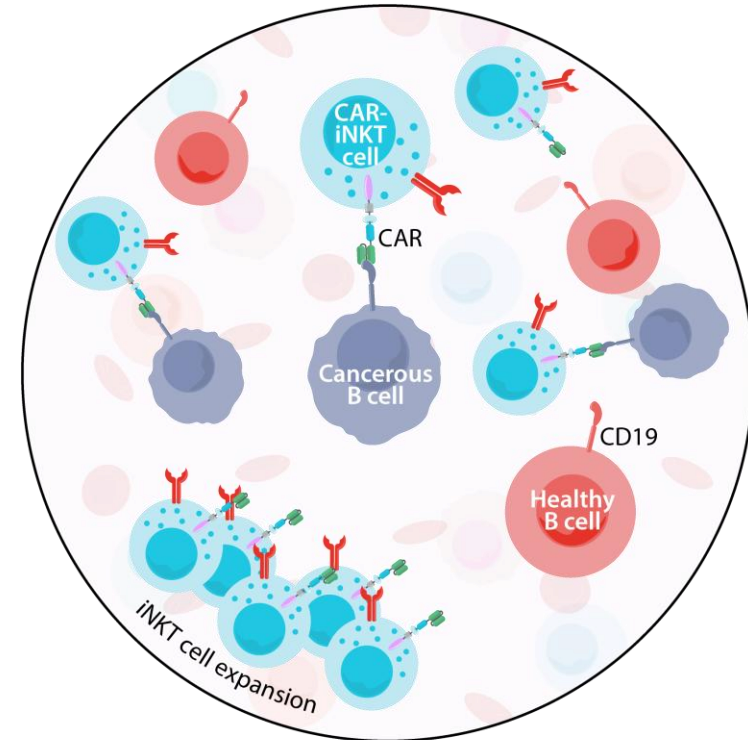
Lack of antigen
specificity and uniformity



Tumour microenvironment
contains cells that support
cancer cell growth



Solid tumour



Blood cancer

iNKT cells:



Home to tissues and infiltrate tumours

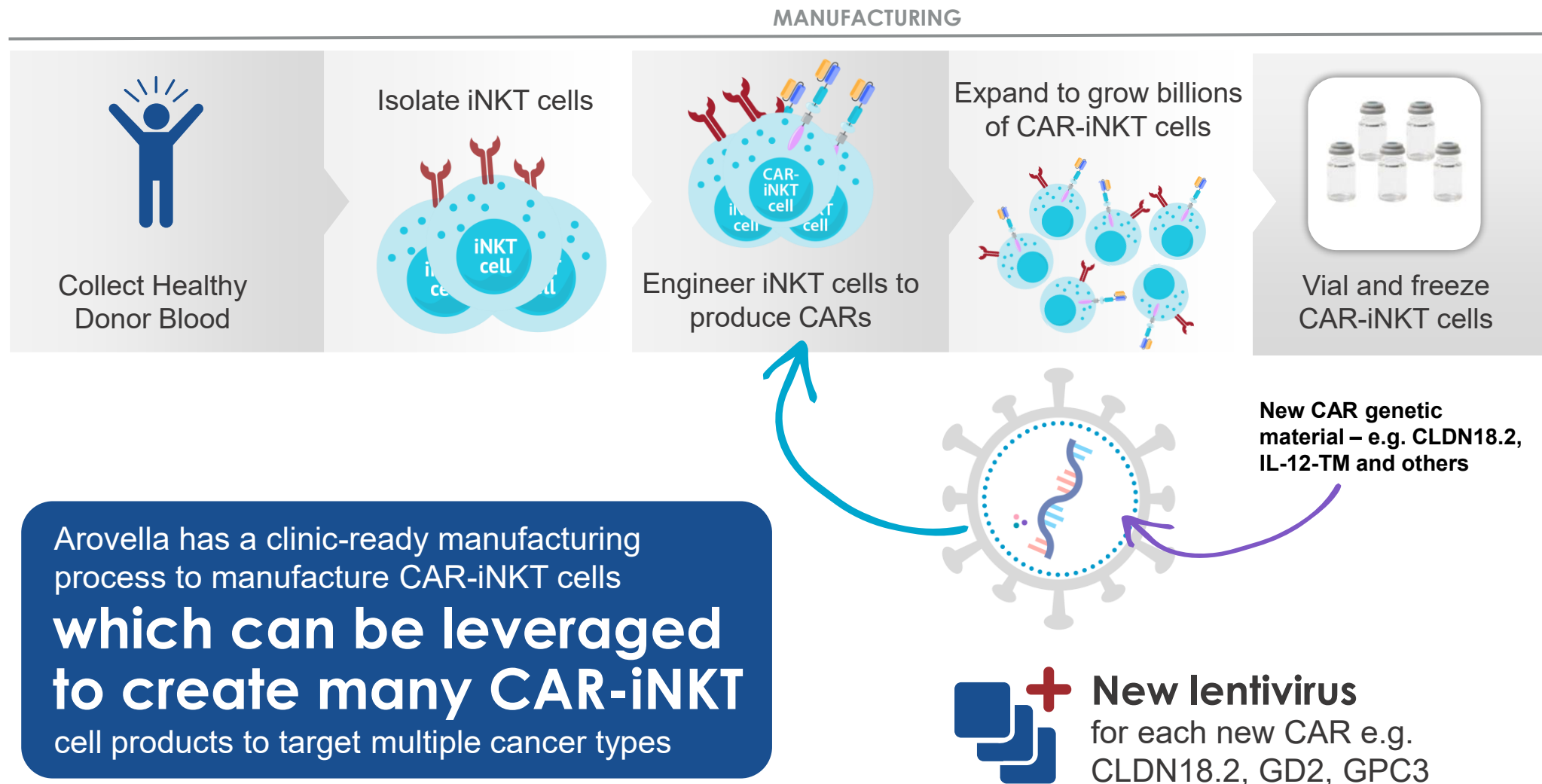


Modify the TME to block or kill cells that promote tumour growth
and recruit helpful immune cells

Add additional CARs for novel targets

New CARs

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



Introducing Claudin 18.2 (CLDN18.2)

A promising solid tumour target

CLDN18.2 overexpression has been
**identified in several
types of cancers**

gastric cancer (GC)

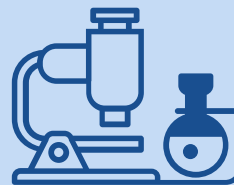
gastroesophageal junction cancer (GEJC)

pancreatic cancer (PC)

esophageal cancer (EC)

ovarian adenocarcinoma (OAC)

lung cancers (LC)



Validated target

with first monoclonal antibody
approved in Japan and the
US in 2024



Gastric cancer

market alone expected to reach
\$10.7 billion by 2031¹



**Successfully
generated
a functional CAR**
that targets CLDN18.2

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

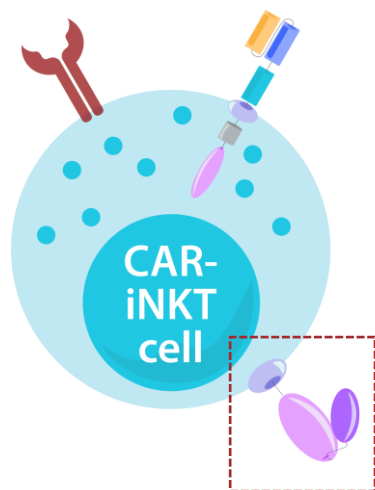
“Armouring” CAR-iNKT cells

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. We have designed it to be attached to the surface of iNKT cells so that 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**

Discover how our IL-12-TM cytokine technology works in our new [IL-12-TM explainer whiteboard video](#).

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

Arovella has entered into a **Sponsored Research Agreement** with Prof. Dotti's group at the University of North Carolina

[nature](#) > [nature communications](#) > [articles](#) > article

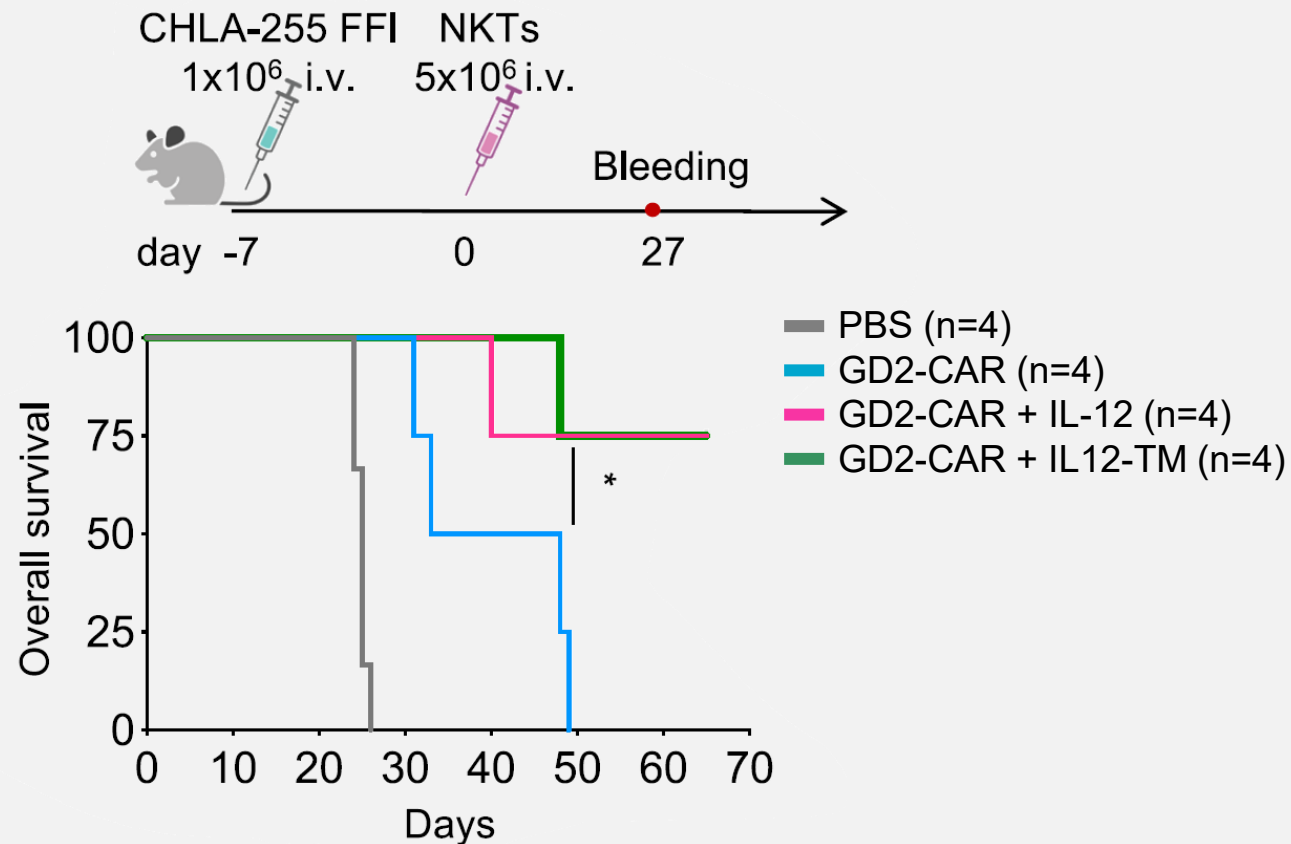
Article | [Open access](#) | [Published: 02 January 2024](#)

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 positive for 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 + IL12 or IL-12-TM remained alive
- IL-12-TM enhances CAR-iNKT cell numbers and antitumour activity
- The GD2 CAR is under Option from Baylor College of Medicine


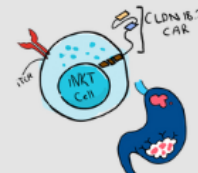



*statistically significant ($p=0.0344$)

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

Arovella's expanding pipeline



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

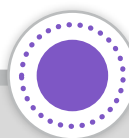
Upcoming milestones for FY2026



Jul
2025



Dec
2025



Jun
2026



ALA-101 (CD19)

- Complete cGMP manufacture and IND enabling studies and file an IND application with US FDA for phase 1
- Complete preparatory activities for a first-in-human phase 1 study for ALA-101 in patients with CD19+ blood cancers

- Commence phase 1 study and generate initial data from patients in early dose cohorts



Arovela is funded to obtain preliminary safety and efficacy readouts for its phase 1 study of ALA-101

ALA-105 (CLDN18.2)

- Integrate the CLDN18.2 CAR into iNKT cells, and optimise the CAR for solid tumours
- Test CLDN18.2 targeting CAR-iNKT cells in gastric cancer and/or pancreatic cancer animal models

- Commence activities to manufacture ALA-105 for clinical trials (e.g. lentiviral vector production)

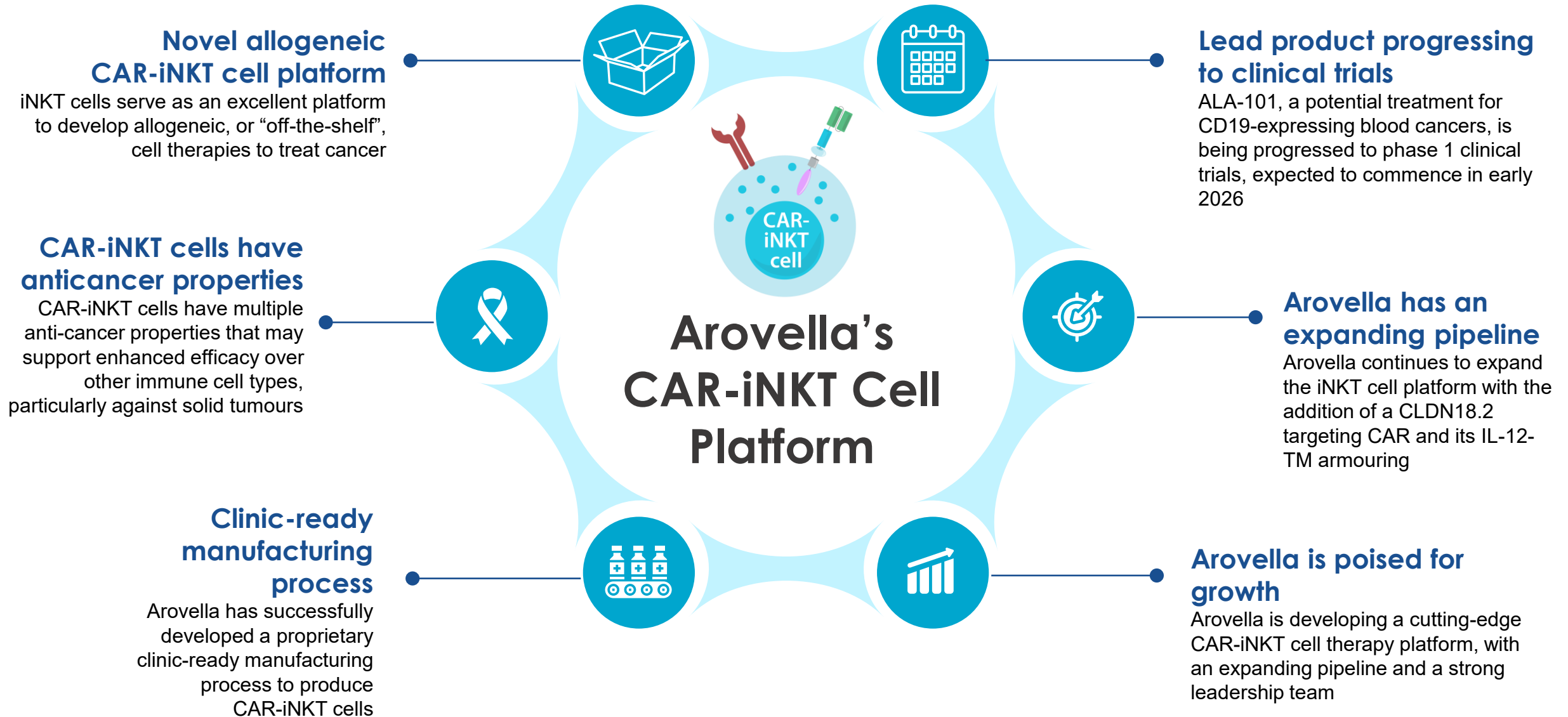
IL-12-TM integration

- Integrate IL-12-TM into solid tumour programs and test its efficacy in anti-tumour models

Pipeline expansion

- Continue to identify and acquire novel technologies that enhance and expand Arovela's iNKT cell therapy platform
- Option with Baylor College of Medicine to be exercised by Nov 2025

Summary



ASX:ALA



Thank You

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Cell therapy deal references



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