ASX: ALAArovella Therapeutics Limited ACN 090 987 250



ASX Release

28 July 2025

INVESTOR PRESENTATION

MELBOURNE, AUSTRALIA 28 July 2025: 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 meetings being conducted this week in Singapore and Hong Kong.

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 **ASX: ALA**Arovella Therapeutics Limited ACN 090 987 250



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 forwardlooking 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.





Non-deal roadshow July

2025



Disclaimer

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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**



Peter Mac ■IQVIA®

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**



Financial overview

Financial Snapshot

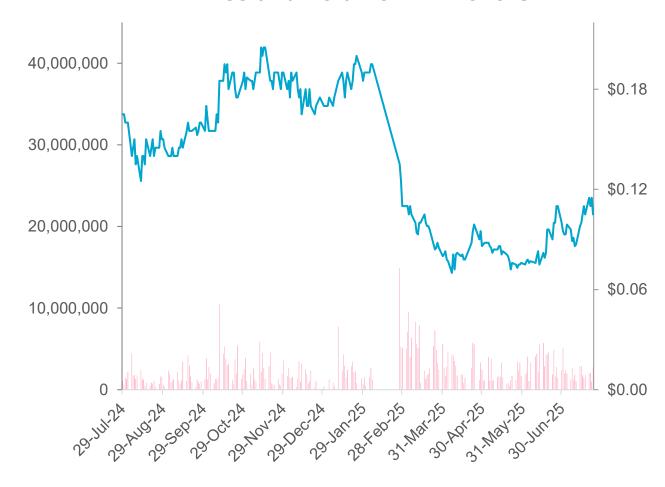
ASX CODE	ALA
Market capitalisation ¹	\$136.7 million
Shares on issue	1,188.6 million
52-week low / high	\$0.068 / \$0.210
Cash Balance (30 Jun, 2025)	\$20.9 million

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 24 July 2025
- 2. As of 21 March 2025
- 3. Holding includes associated entities and parties

ALA Price and Volume - 12 Months¹



Recent cell therapy transactions¹

Date	Type of deal	Acquirer/Licensee	Target/Licensor	Cell Type	Stage	Upfront (US\$M)	Milestones (US\$M)	Total deal value (US\$M)
Jun-25	Acquisition	abbvie	€capstan tx**	In vivo CAR	Phase 1	\$2,100	\$0	Up to \$2,100
Mar-25	Acquisition	AstraZeneca 2	EsoBiotec	In vivo CAR	Phase 1	\$425	\$575	\$1,000
Nov-24	Acquisition	Roche	POSEIDA	Allo T cell	Phase 1	~\$1,038	~\$462	\$1,500
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 J	CBMG Cellular Biomedicine Group	T Cell	Phase 1b	\$245	undisclosed	
Jan-23	Acquisition	AstraZeneca 🕏	neo gene	T Cell	Phase 1	\$200	\$120	\$320
Oct-22	Development collaboration ⁵	GILEAD	ARCELLX	T Cell	Phase 2	\$225	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

ASX:**ALA**

^{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

Highlights for CY 2025 to date...



Cash and cash equivalents at 30 June, 2025 of

\$20.9 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





About CAR-T cells

Cell Therapy has revolutionised blood cancer treatment

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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

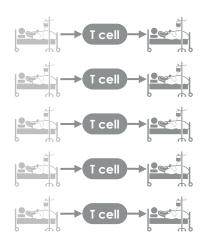
Product App	oroval Year	2024 Revenue
YESCARTA* (axicabtagene ciloleucel) Supression	2017	US\$1570m ³
(tisagenlecleucel) for printing	2017	US\$442m ⁴
Abecma* (idecabtagene vicleucel) ####################################	2021	US\$242m ⁵

- https://www.businesswire.com/news/home/20230529005130/e n/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
- https://www.gilead.com/news/news-details/2025/gileadsciences-announces-fourth-quarter-and-full-year-2024financial-results.
- https://www.novartis.com/sites/novartis_com/files/2025-01interim-financial-report-en.pdf
- https://ir.2seventybio.com/news-releases/news-releasedetails/2seventy-bio-reports-preliminary-full-year-us-abecmasales-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

3-4 weeks for therapy



- Manufacturing & supply chain costs are high
- T cells <u>can be</u> <u>compromised</u> due to disease
- Limited centres can collect and manufacture
- for patients with aggressive disease
- Manufacturing run failures can occur

ALA's solution: One CAR-iNKT batch from a healthy donor treats multiple patients



CAR-INKT

cell

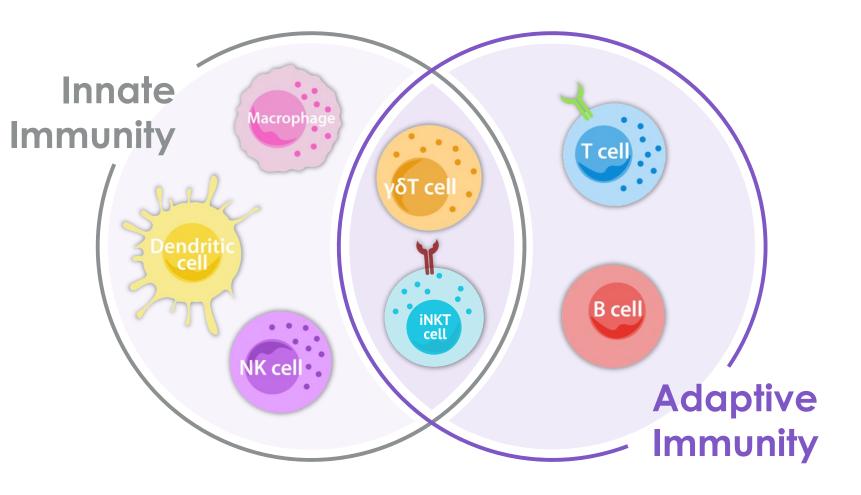
Patients ready to dose within 1 week



Introducing invariant Natural Killer T (iNKT) cells



Bridging the innate and adaptive immune system

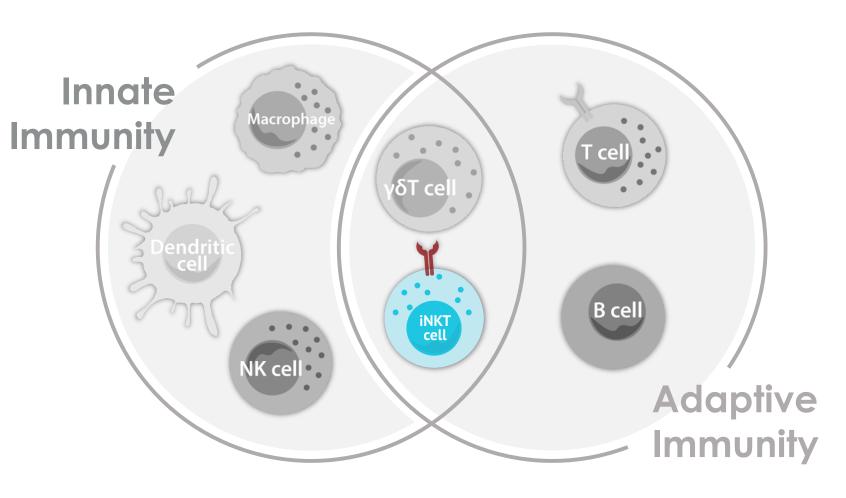




iNKT cells represent a next-generation cell therapy

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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

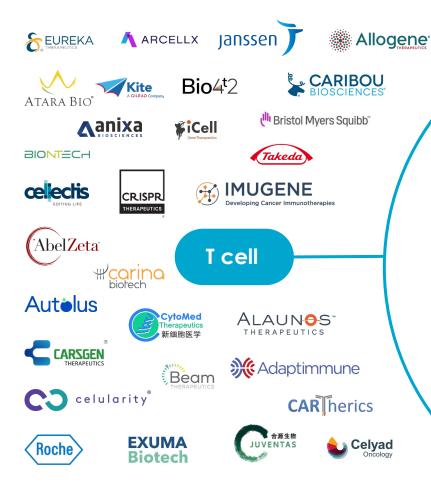
Multiple anti-cancer properties

- 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

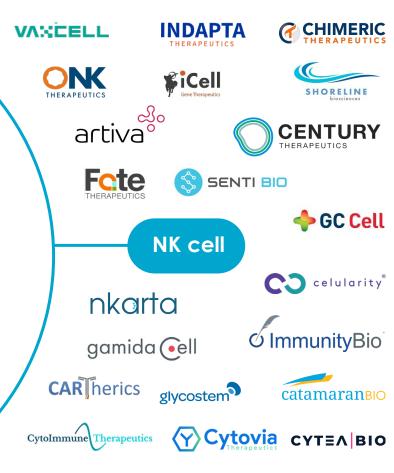




inkeso

Biotherapeutics

** APPIA BIO







ALA-101 (CAR19-iNKT cells)

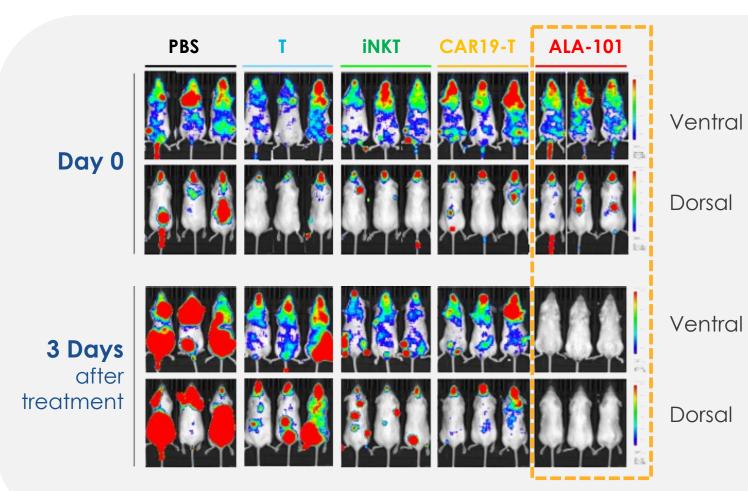
A next generation **off-the-shelf** cell therapy for CD19 expressing cancers

ALA-101: enhanced tumour killing in vivo

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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



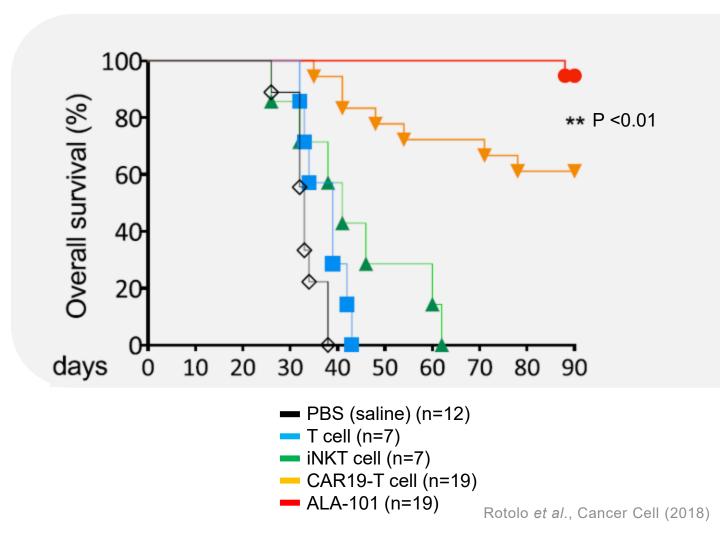
Rotolo et al., Cancer Cell (2018)

ALA-101: next generation cell therapy

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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

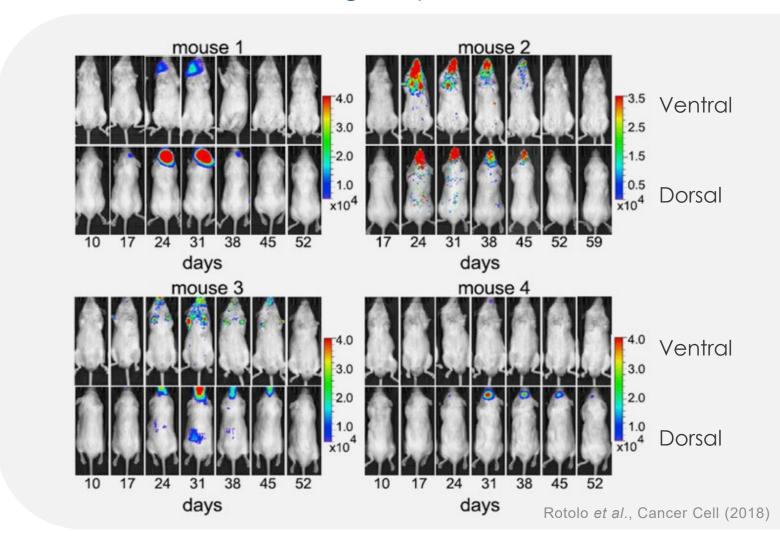


ALA-101: spontaneous secondary remission



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



Clinic-ready manufacturing process developed

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

TECHNOLOGY ACQUISITION

PRE-CLINICAL CONFIRMATION

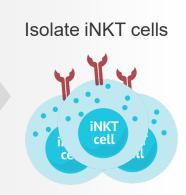
LENTIVIRUS MANUFACTURING

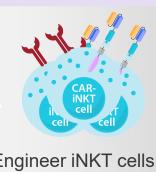
MANUFACTURING PLATFORM

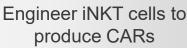
FDA (IND) / TGA (CTA) PHASE 1 CLINICAL TRIAL

PHASE 2 CLINICAL TRIAL

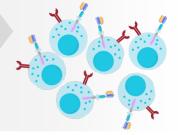














Progressed tech transfer to the GMP suites for clinical manufacturing

- 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

Taking ALA-101 into first-in-human trials

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

KOL engagement and Clinical trial design

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

Clinical Advisory Board meeting held

Ongoing

IND-enabling studies and regulatory submission

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

In vivo animal model completed

Regulatory approval and site startup

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













First Patient Dosed

Ongoing

GMP manufacturing of clinical drug product

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

Runs completed in GMP suites with GMP reagents

Ongoing

Selection of clinical sites and CRO

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



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



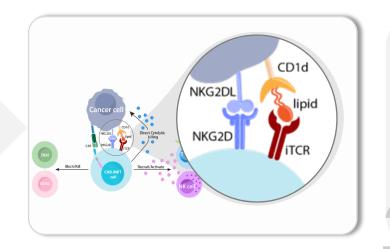


iNKT cells are naturally well placed to target solid tumours

iNKT cells have features that provide advantages in the complex solid tumour environment

Naturally target cancer markers and are prognostic for survival

iNKT cells naturally target CD1d, NKG2DL and other markers present on some tumour types. iNKT cell levels are prognostic for colorectal cancer and head and neck squamous cell carcinoma.^{1,2}

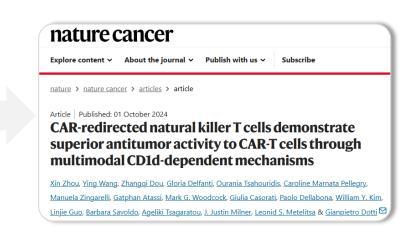


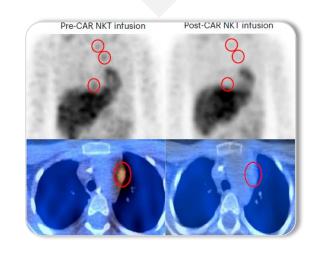
Infiltrate tumours and have shown promising clinical data in human solid tumour studies

iNKT cells have been shown to infiltrate solid tumours and have shown promising data when tested in human clinical studies for a range of solid tumours, including neuroblastoma and renal cell carcinoma.^{5,6}

Kill pro-tumour cells, activate helpful immune cells and outperform CAR-T cells

iNKT cells can influence the TME, induce cross-priming of other immune cells³, and CAR-iNKT cells have been shown to outperform CAR-T cells when tested using mouse models.⁴







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

Create partnerships to use novel combination therapies with synergistic effects

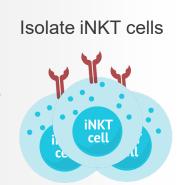
Add additional CARs for novel targets

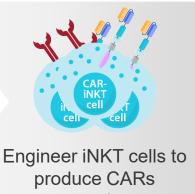
New CARs

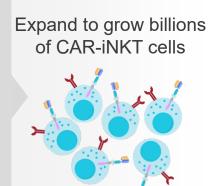
Arovella's manufacturing process can be leveraged for multiple cancer types

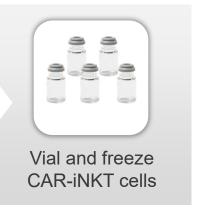
MANUFACTURING









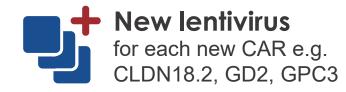


New CAR genetic material – e.g. CLDN18.2, IL-12-TM and others

Arovella has a clinic-ready manufacturing process to manufacture CAR-iNKT cells

which can be leveraged to create many CAR-iNKT

cell products to target multiple cancer types



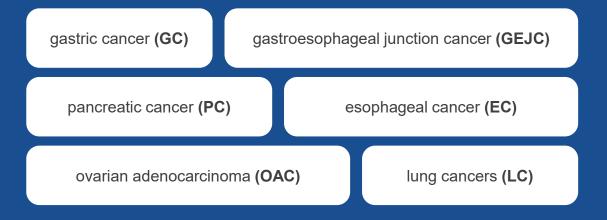
Introducing Claudin 18.2 (CLDN18.2)

O

A promising solid tumour target

CLDN18.2 overexpression has been

identified in several types of cancers





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

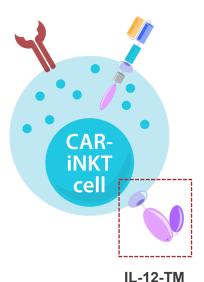
ARMOURING

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"Armouring" CAR-iNKT cells

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

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

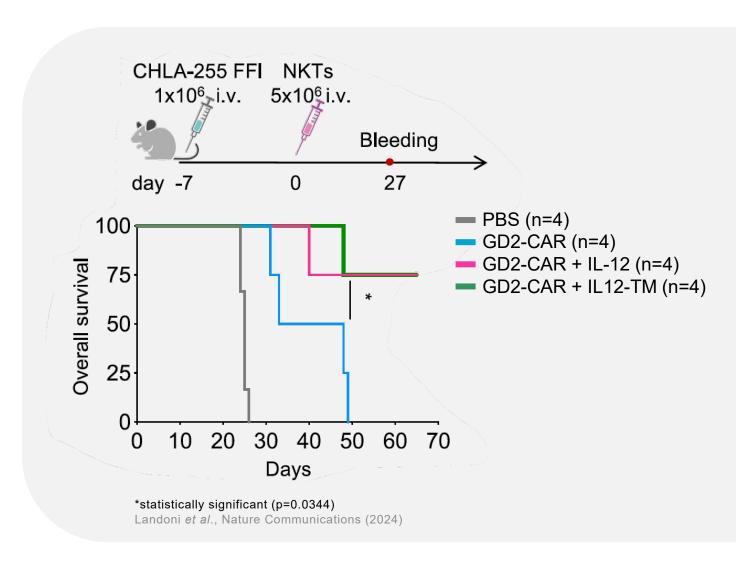
Article Open access Published: 02 January 2024

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

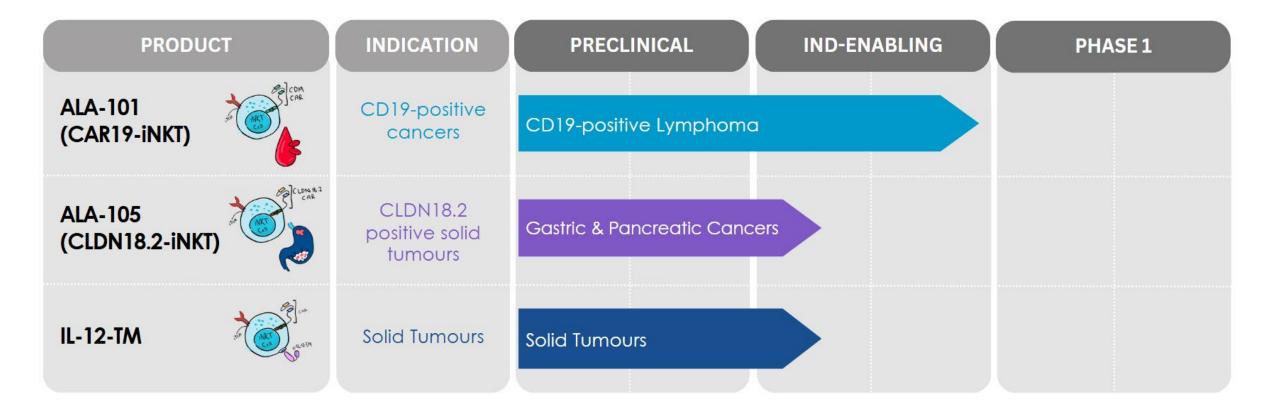
- Tumour cells positive for GD2 and were intravenously delivered into mice before treatment with CAR-iNKT cells
- Mice were treated with:
 - PBS (saline)
 - GD2-CAR
 - GD2-CAR + IL-12
 - GD2-CAR + IL-12-TM
- After 60 days, only mice treated with GD2-CAR + IL12 or IL-12-TM remained alive
- II -12-TM enhances CAR-iNKT cell numbers and antitumour activity





Arovella's expanding pipeline







Upcoming milestones for FY2026



Jul 2025

Dec **2025**

Jun **2026**



- 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



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



(CD19)

- 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 Arovella's iNKT cell therapy platform
- Option with Baylor College of Medicine to be exercised by Nov 2025



Summary



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

CAR-iNKT cells have anticancer properties

CAR-iNKT cells have multiple anti-cancer properties that may support enhanced efficacy over other immune cell types, particularly against solid tumours



Arovella's **Platform**

Clinic-ready manufacturing process

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



O



INKT

cell



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 early 2026

Arovella has an expanding pipeline

Arovella continues to expand the iNKT cell platform with the addition of a CLDN18.2 targeting CAR and its IL-12-TM armouring

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







Thank You Dr. Michael Baker CEO & Managing Director

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Cell therapy deal references

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