

ASX:ALA



# Investor Presentation

## Singapore Healthcare Day

March 2024

Spark+



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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, a potential treatment for CD19-expressing blood cancers, is 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 the iNKT cell therapy platform and align with core focus areas

## Unique Value Proposition

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



# Financial overview

## Financial Snapshot

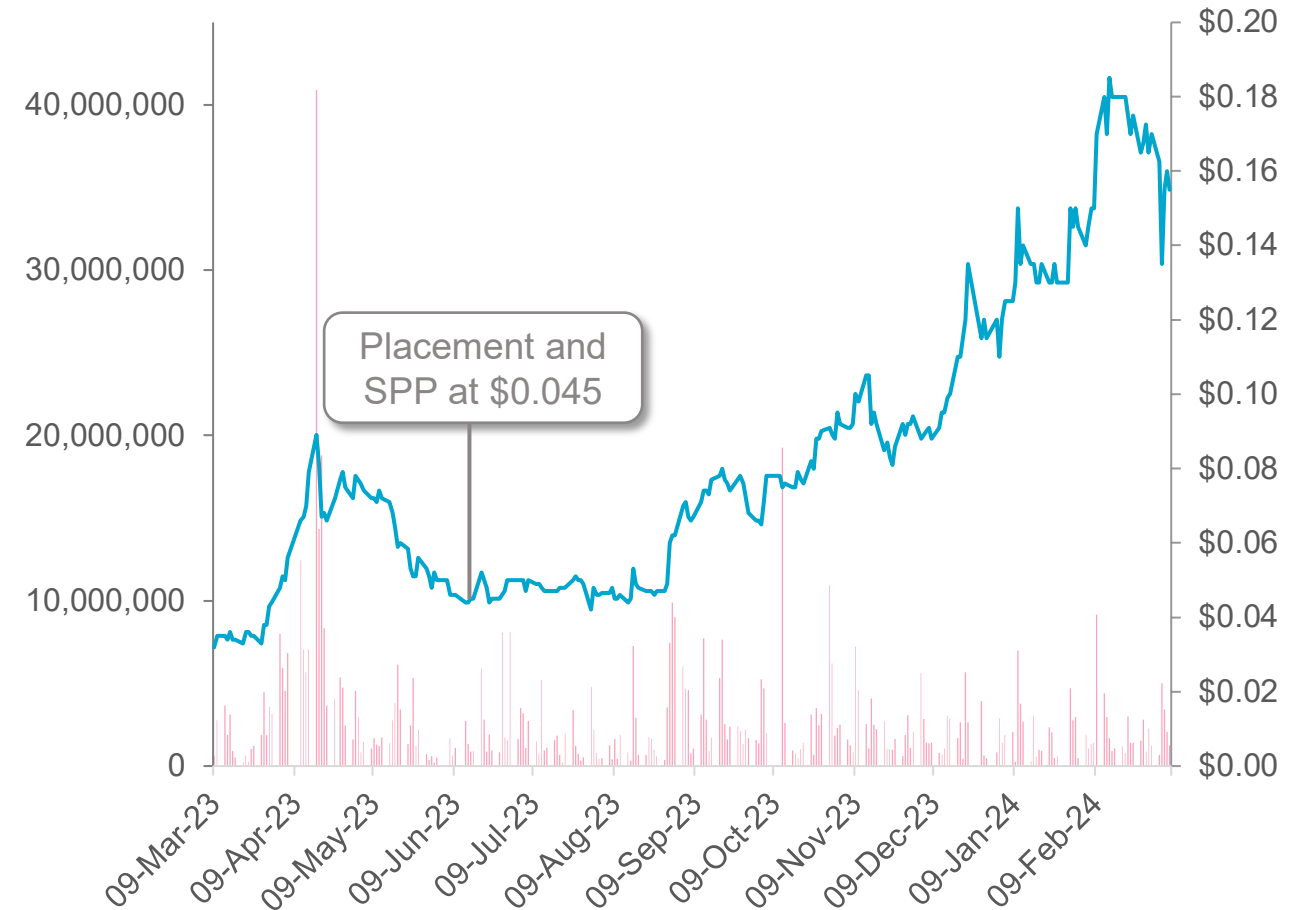
ASX CODE	ALA
Market capitalisation <sup>1</sup>	\$143.4 million
Shares on issue	925.1 million
52-week low / high <sup>1</sup>	\$0.033 / \$0.185
Cash Balance (Dec 31 2023)	\$4.76 million

## Major Shareholders

Shareholder	Ownership (%) <sup>1</sup>
THE TRUST COMPANY (AUSTRALIA) LIMITED	56,186,926 (6.12%)
RICHARD JOHN MANN	50,905,657 (5.54%)
UBS NOMINEES PTY LTD	20,620,196 (2.25%)
BLACKBURNE CAPITAL PTY LTD	18,407,456 (2.00%)
DYLIDE PTY LTD	15,666,666 (1.71%)



























1. As of 8 March 2024

## ALA Price and Volume - 12 Months<sup>1</sup>





# Recent cell therapy transactions<sup>1</sup>

Date	Type of deal	Acquirer/Licensee	Target/Licensors	Cell Type	Stage	Upfront (US\$M)	Milestones (US\$M)	Total deal value (US\$M)
Dec-23	Acquisition	 AstraZeneca	 GRACELL	T Cell	Phase 1b	\$1,000	\$200	\$1,200
Nov-23	Collaboration and investment <sup>2</sup>	 AstraZeneca	 cellectis	Not specified	Platform	\$25	\$70-220 per product	
Aug-23	Licence <sup>3</sup>	 IMUGENE <small>Developing Cancer Immunotherapies</small>	 PRECISION BIOSCIENCES	T Cell	Phase 1b	\$21	\$206	\$227
Aug-23	Strategic investment (ROFR) <sup>4</sup>	 astellas	 POSEIDA THERAPEUTICS	T Cell	Phase 1	\$25	\$0	\$25
May-23	Licence	 janssen	 CBMG <small>Cellular Biomedicine Group</small>	T Cell	Phase 1b	\$245	<i>undisclosed</i>	
Jan-23	Acquisition	 AstraZeneca	 neogene THERAPEUTICS	T Cell	Phase 1	\$200	\$120	\$320
Oct-22	Development collaboration <sup>5</sup>	 GILEAD	 ARCELLX	T Cell	Phase 2	\$225	<i>undisclosed</i>	
Sep-22	Research collaboration	 Genentech <small>A Member of the Roche Group</small>	 ArsenalBio	T Cell	Preclinical	\$70	<i>undisclosed</i>	
Aug-22	Licence & strategic collaboration	 Roche	 POSEIDA THERAPEUTICS	T Cell	Phase 1	\$110	\$110	\$220
Sep-21	Development collaboration	 Genentech <small>A Member of the Roche Group</small>	 Adaptimmune	T Cell	Preclinical	\$150	\$150	\$300
Aug-21	Research collaboration	 GILEAD	 APPIA BIO	iNKT Cell	Preclinical	<i>undisclosed</i>	<i>undisclosed</i>	\$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 final 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

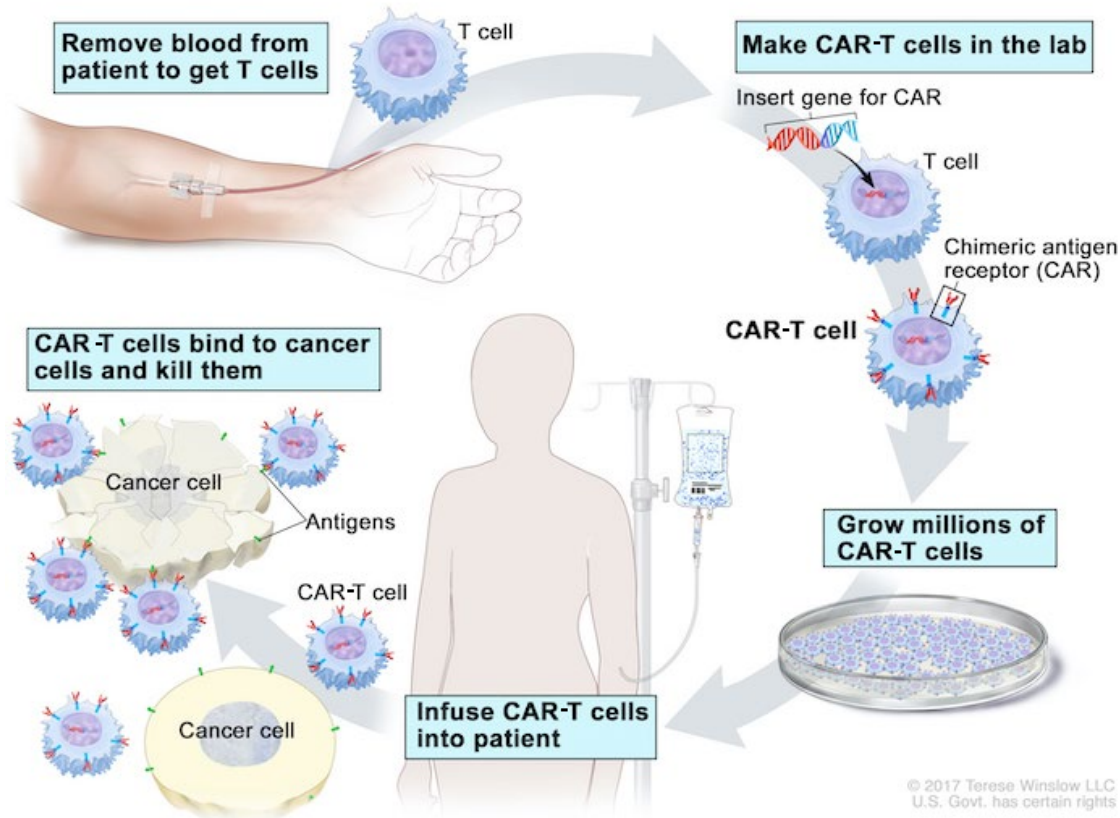
3. Precision is eligible for double digit royalties on net sales and \$145 million in milestone payments and tiered royalties for additional programs

4. Poseida also received a US\$25m equity investment from Astellas

5. Arcellx also received a US\$100m equity investment from Gilead

# How original CAR-T cell therapies work

CAR-T cell therapy is personalised medicine



## T cells = immune cell

T cells are a common type of immune cell that fight infections and can help fight cancer.



## T cells from patient 'reprogrammed'

To generate autologous CAR-T cells, T cells are taken from a patient with blood cancer and 'reprogrammed' to produce a Chimeric Antigen Receptor (CAR). The CAR can recognise cancer cells through a target antigen.



## CAR-T cells find & kill tumour cells

CAR-T cells are administered to the patient to find and kill the tumour cells. Once the CAR binds to a tumour cell, the CAR-T cell is activated to kill the tumour cell.

# 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 2030<sup>1</sup>

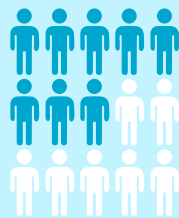


## Cure

CAR-T cells have demonstrated ability to cure haematological cancers



## Strong Sales



**40-60%**

Patients relapse post-CAR-T therapy<sup>2</sup>

Product	Approval Year	2023 Revenue
 <b>YESCARTA</b> (axicabtagene ciloleucel) <sup>3</sup>	2017	US\$1498m <sup>3</sup>
 <b>KYMRIAH</b> (tisagenlecleucel) <sup>4</sup>	2017	US\$509m <sup>4</sup>
 <b>Abecma</b> (idecabtagene vicleucel) <sup>5</sup>	2021	US\$472m <sup>5</sup>

- <https://www.businesswire.com/news/home/20230529005130/en/Global-Cell-Therapy-Market-Report-2023-Advancements-in-Biotechnology-Drives-Growth---ResearchAndMarkets.com>
- Zinzi et al., 2023 Pharmacological Research - 10.1016/j.phrs.2023.106742
- [https://www.gilead.com/news-and-press/press-room/press-releases/2024/2/gilead-sciences-announces-fourth-quarter-and-full-year-2023-financial-results#:~:text=Yescarta%C2%AE%20\(axicabtagene%20ciloleucel\)%20sales,%E2%80%9D\)%20outside%20the%20United%20States.](https://www.gilead.com/news-and-press/press-room/press-releases/2024/2/gilead-sciences-announces-fourth-quarter-and-full-year-2023-financial-results#:~:text=Yescarta%C2%AE%20(axicabtagene%20ciloleucel)%20sales,%E2%80%9D)%20outside%20the%20United%20States.)
- [https://www.novartis.com/sites/novartis\\_com/files/2024-01-interim-financial-report-en.pdf](https://www.novartis.com/sites/novartis_com/files/2024-01-interim-financial-report-en.pdf)
- <https://news.bms.com/news/details/2024/Bristol-Myers-Squibb-Reports-Fourth-Quarter-and-Full-Year-Financial-Results-for-2023/default.aspx>





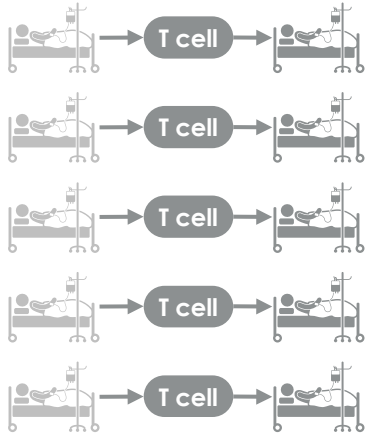
Emily Whitehead - Celebrating 10 years of CAR-T cell therapy

<https://emilywhiteheadfoundation.org/10-years-of-car-t/>



# Autologous CAR-T pose challenges

The current manufacturing costs and time are limiting



Each manufacturing batch is **patient-specific**

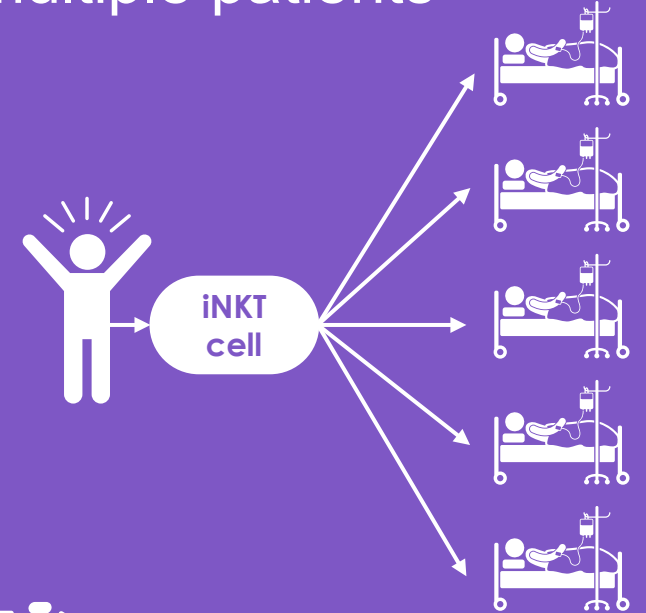
Patient must wait **3-4 weeks** for therapy



- ❗ 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**

# Allogeneic

A single healthy donor batch = treatment for multiple patients

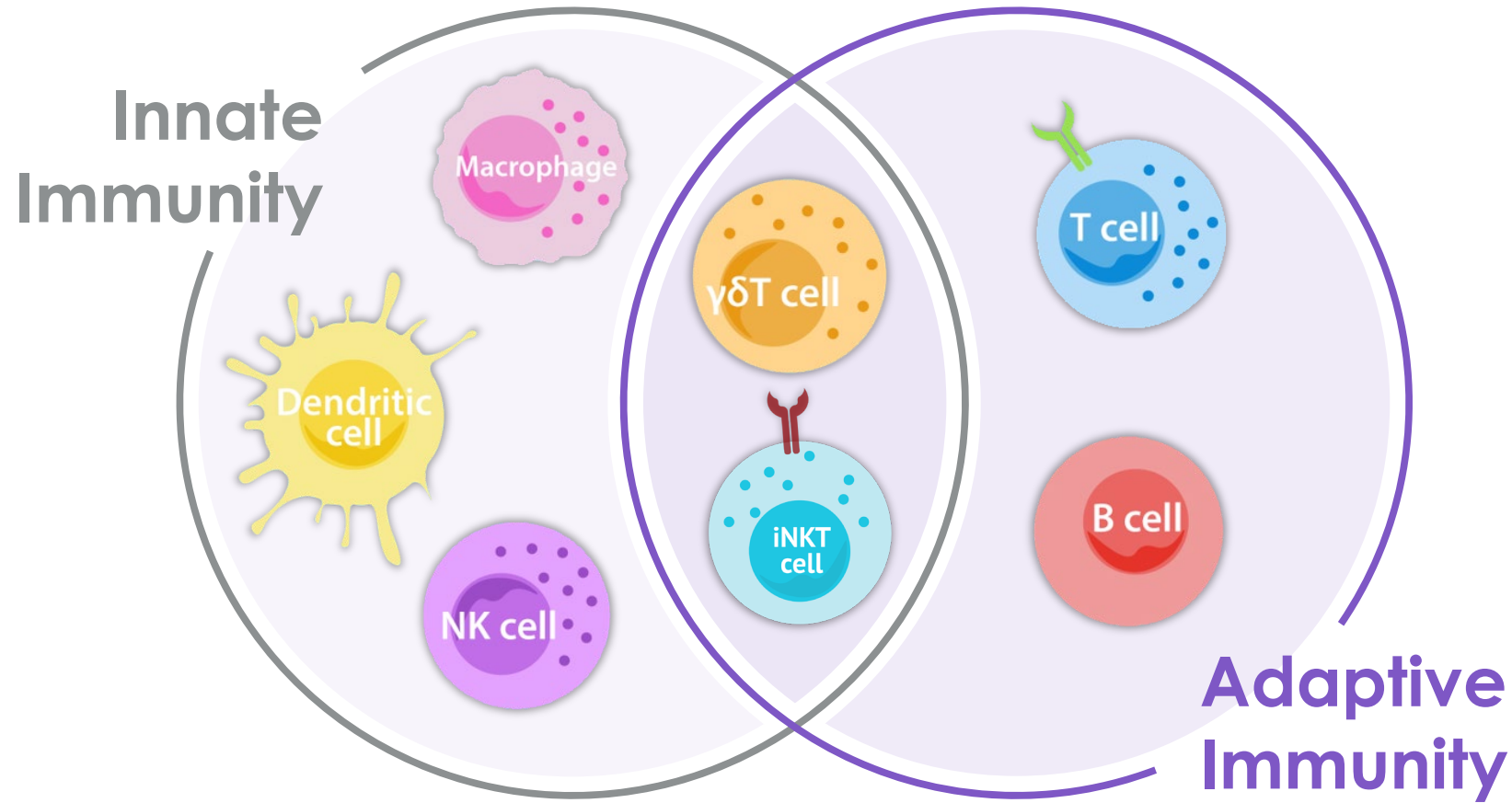


 **1 week**

Patients ready to dose within 1 week

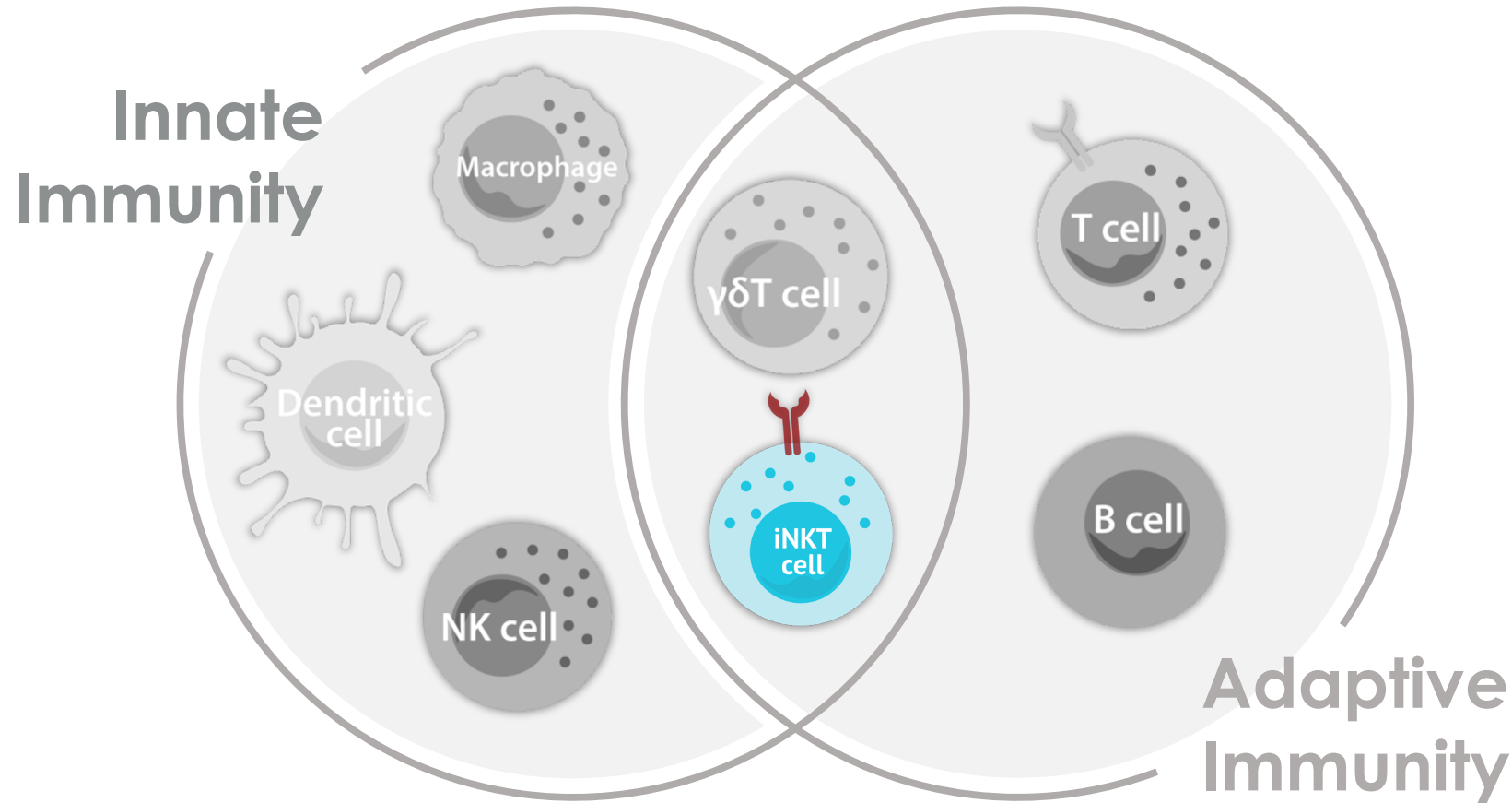
# Introducing invariant Natural Killer T (iNKT) cells

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

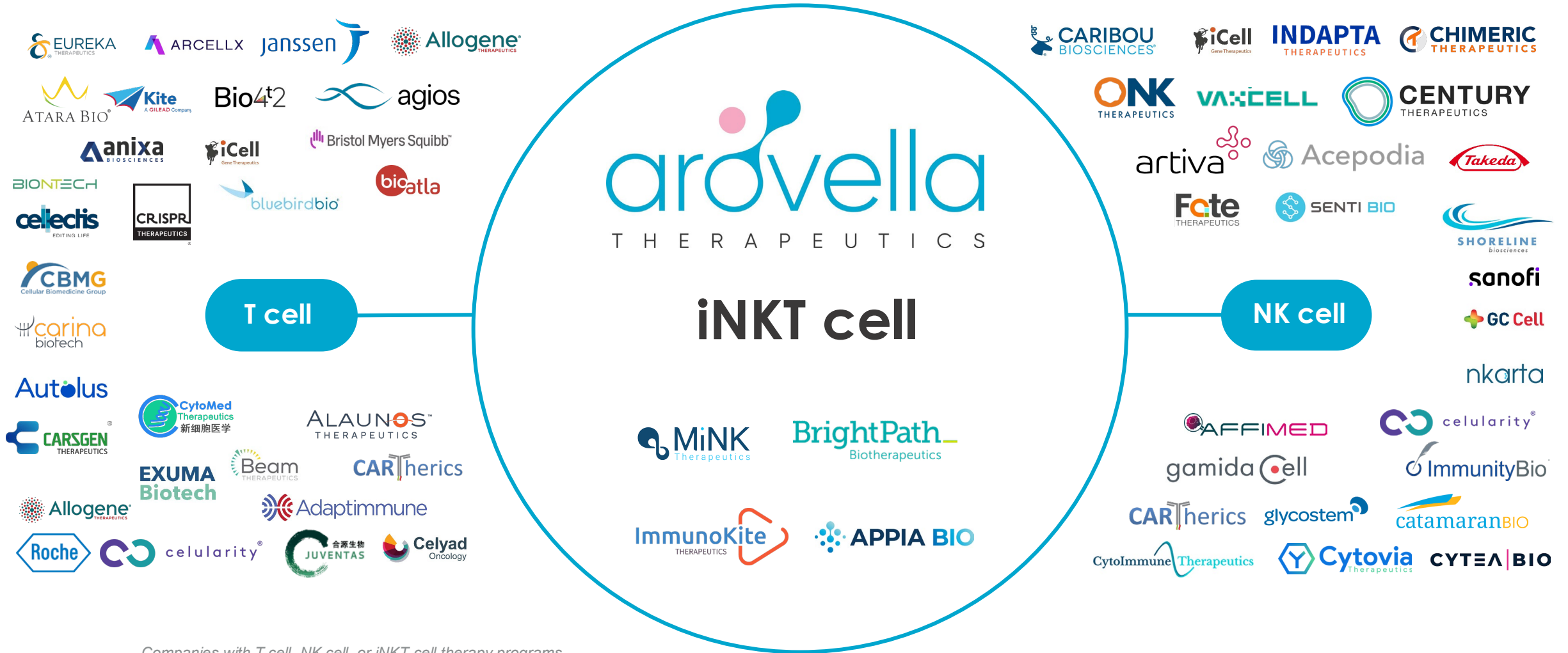
## Multiple anti-cancer properties

- 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



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

# CAR-iNKT cell therapy production advantages

## Off-the-shelf manufacturing advantages

### MANUFACTURING

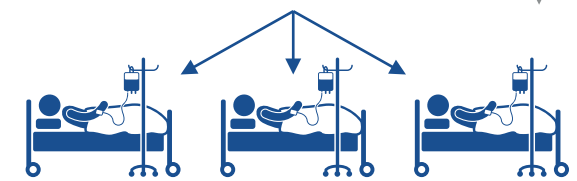


TREATMENT

Thaw CAR-iNKT cells



Dose eligible patients



**Healthier starting material**  
Potentially better efficacy



**Scalable manufacturing with reduced costs**  
Reach more patients



**Faster access to treatment**  
Improved outcomes for aggressive cancers



**Removes risk of manufacturing run failure**  
Stored frozen, ready for use



# ALA-101 (CAR19-iNKT cells)

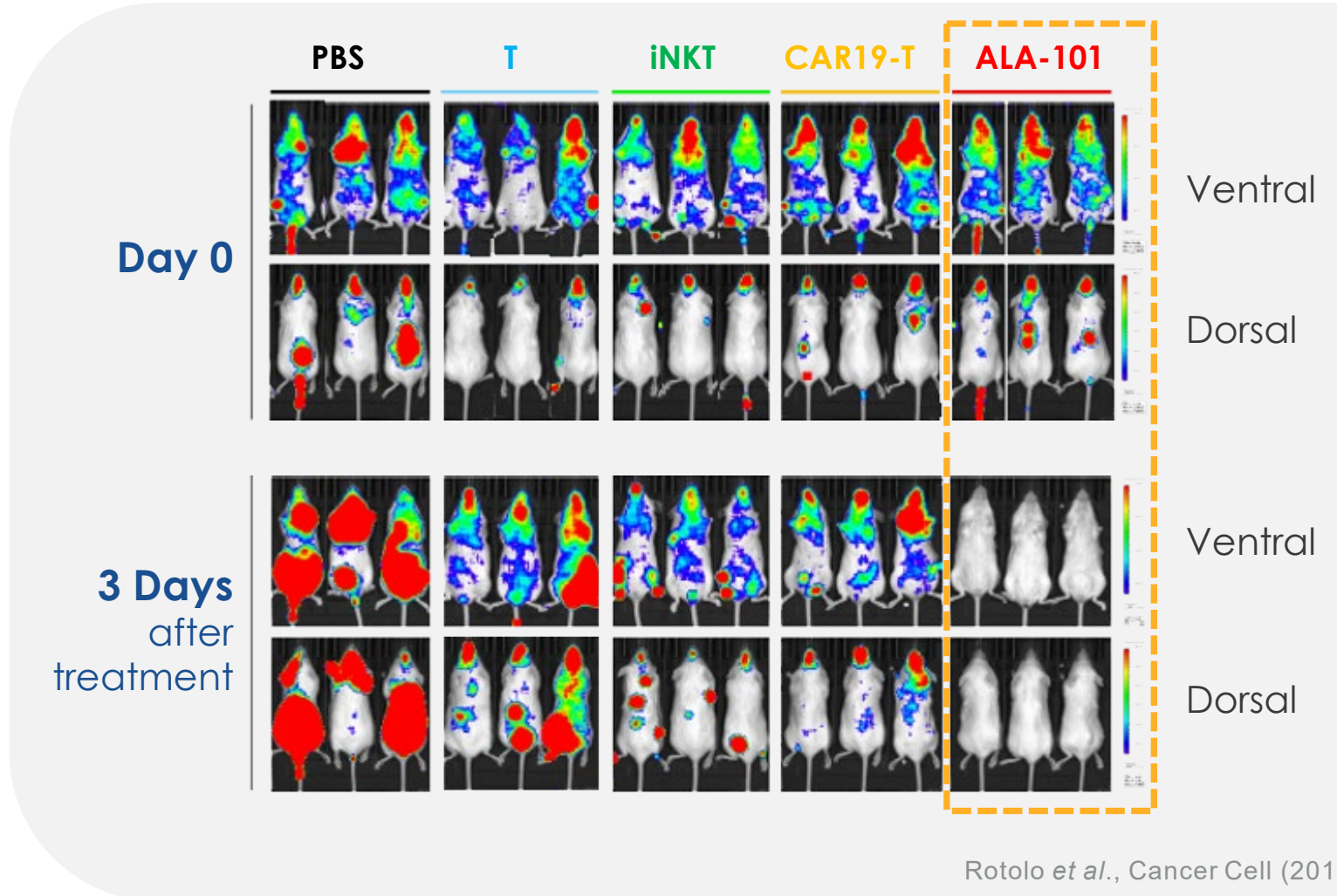
A next generation **off-the-shelf**  
cell therapy for CD19  
expressing cancers



# ALA-101: enhanced tumour killing *in vivo*

ALA-101 rapidly eradicates tumour cells in mice

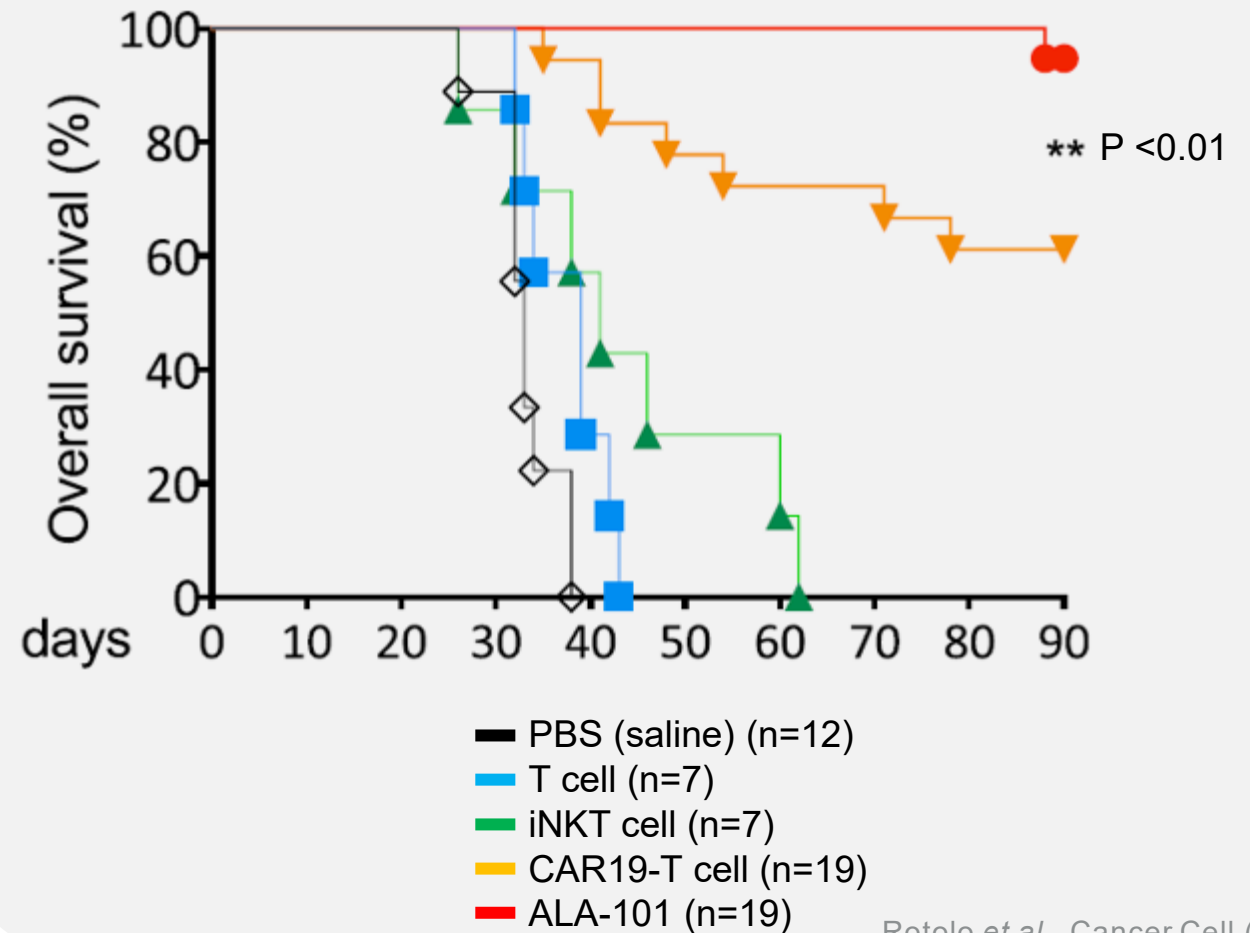
- Tumour cells expressing **CD19** and **CD1d** were intravenously delivered into mice
- Mice were treated with:
  - PBS (saline)
  - Unmodified T cells (T)
  - Unmodified iNKT cells (iNKT)
  - CAR19-T cells
  - ALA-101 (CAR19-iNKT cells)
- After three days, ALA-101 resulted in significant regression of tumour cells
- In all other treatments, there was strong tumour cell persistence
- ALA-101 displays swift action



# 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

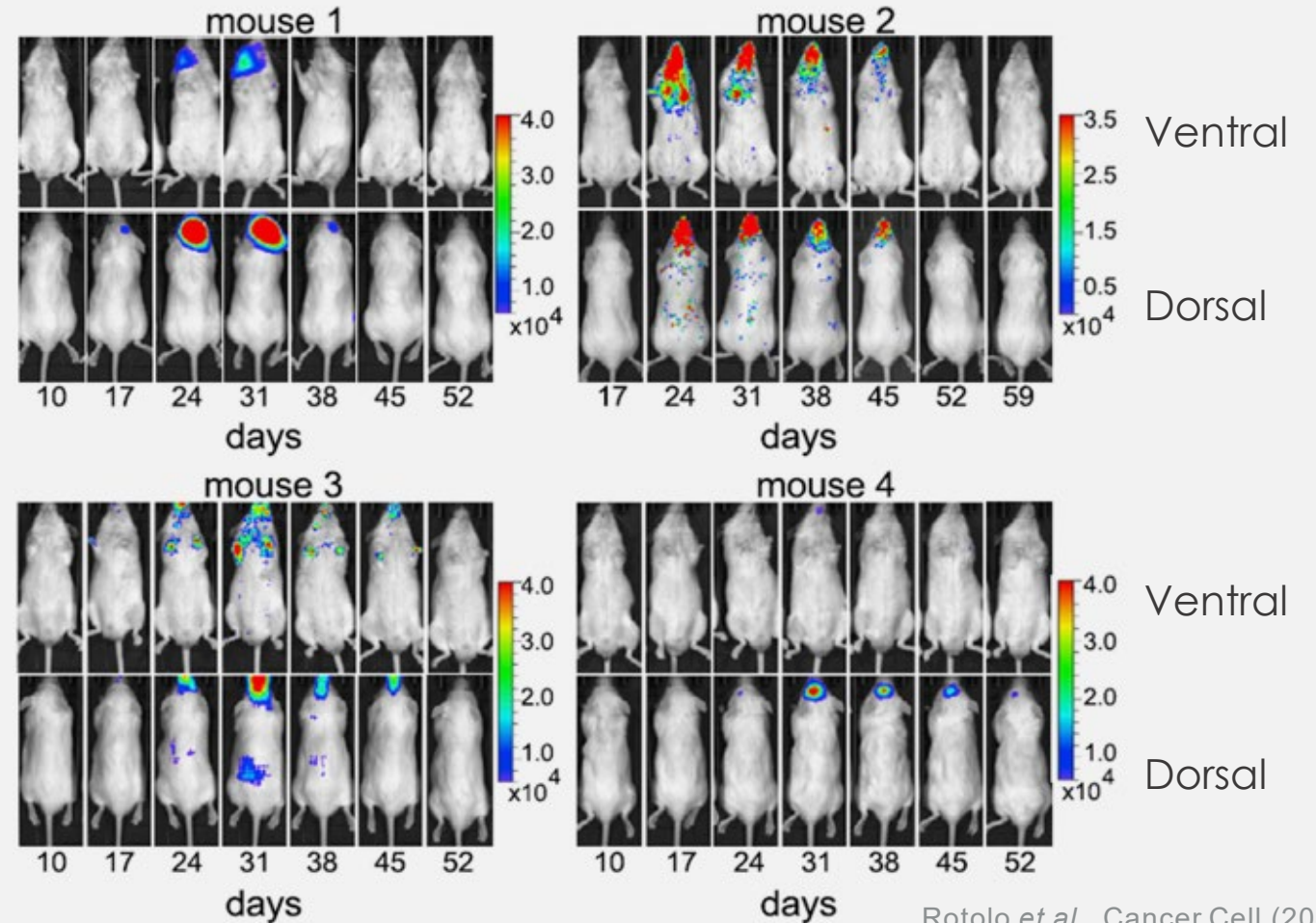


Rotolo et al., Cancer Cell (2018)

# 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)



# Progress towards first-in-human clinical trials

ALA-101 data confirms activity and off-the-shelf capability

## Potent antitumour activity

Demonstrated efficacy of ALA-101 against CD19+ lymphomas and leukemias. Proof-of-concept data with clinical-designed lentiviral vector in animal models using thawed, “off-the-shelf” ALA-101.



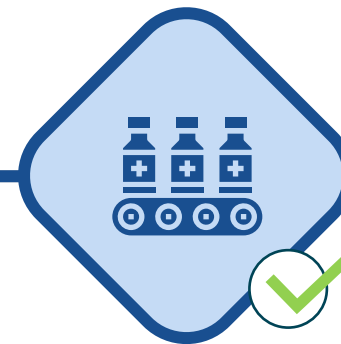
## Expected to be safe

iNKT cells have been shown in clinical trials not to cause graft versus host disease (GvHD) and the CD19 targeting CAR (FMC63) is a validated targeting agent in approved cell therapies.

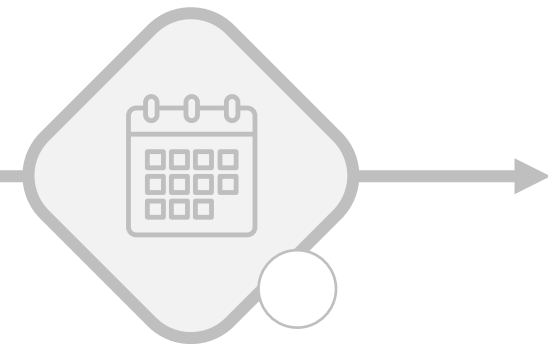
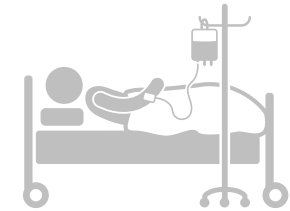


## Multiple dose manufacturing

ALA has demonstrated that its manufacturing process can produce a high number of CAR+ cells with potent cell killing properties and has completed production of GMP-grade lentivirus for CD19 CAR expression.



Phase 1 clinical trial anticipated CY 2024



# iNKT cells to target solid tumours

Arovella is implementing its strategy to target and kill solid tumours – 90% of newly diagnosed cancer cases<sup>1</sup>

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

# Solid tumours pose challenges to cell therapies



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



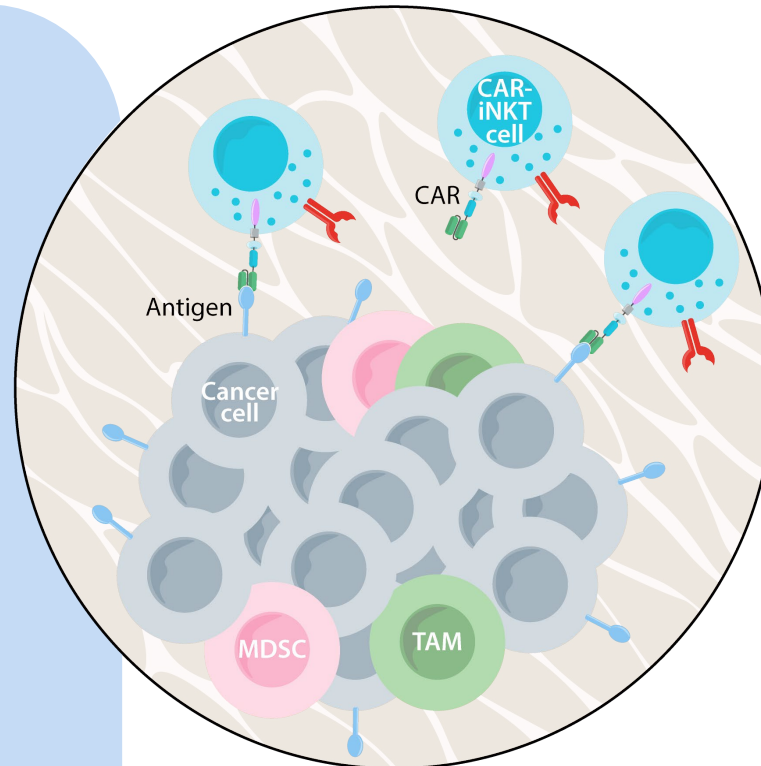
Access to tumour



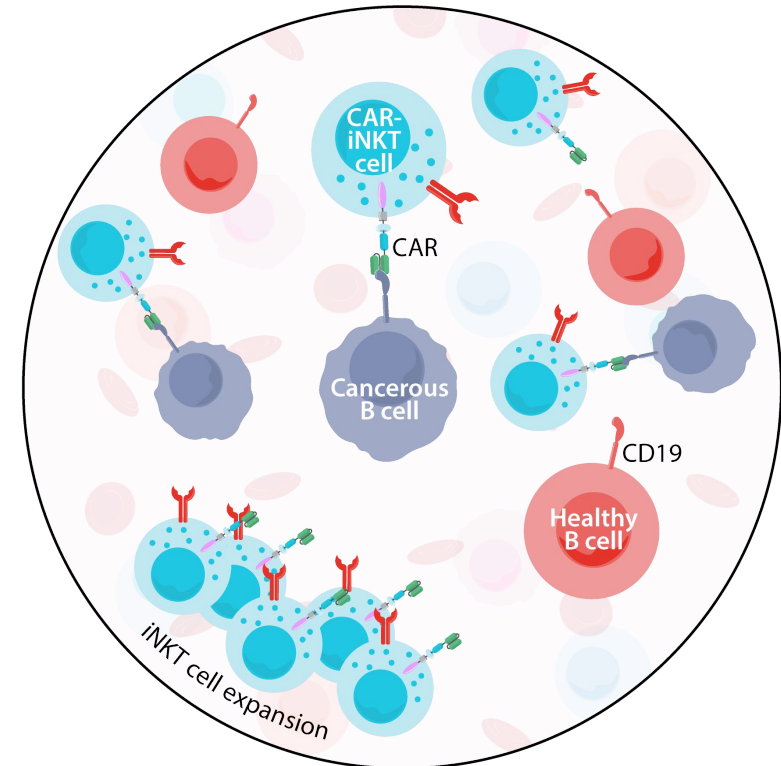
Antigen specificity and uniformity



Tumour microenvironment (TME) 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

# 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

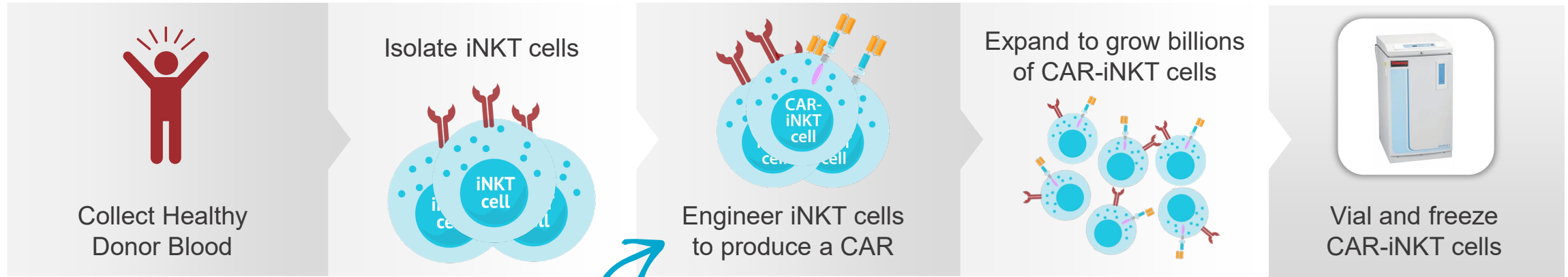
Create partnerships to use novel combination therapies with synergistic effects



# Add additional CARs for novel targets

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

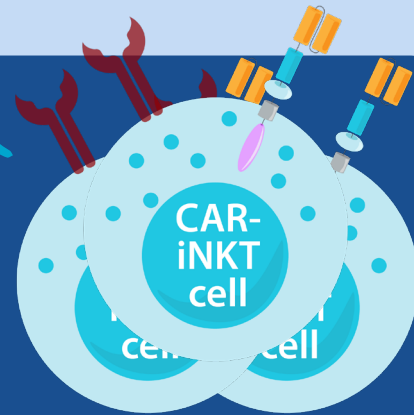
## MANUFACTURING



CARs targeting novel antigens specific for solid tumours

**can be incorporated into iNKT cells**

using the same manufacturing process



**+** New lentiviral vector generated for each new CAR

# 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)

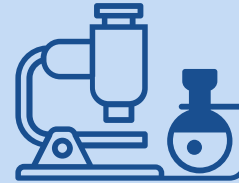
gastroesophageal junction cancer (GEJC)

pancreatic cancer (PC)

esophageal cancer (EC)

ovarian adenocarcinoma (OAC)

lung cancers (LC)



## Validated target

with first monoclonal antibody expected to be **approved in 2024**



## Gastric cancer

market alone expected to reach **\$10.7 billion** by 2031<sup>1</sup>

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

# “Armouring” CAR-iNKT cells

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

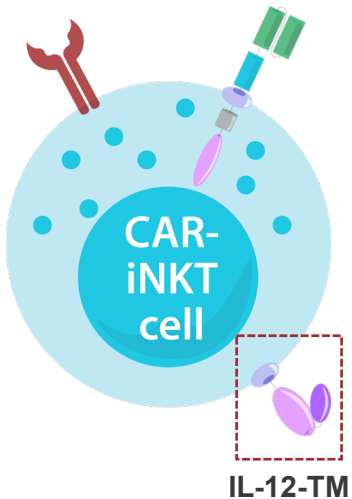
## IL-12-TM

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

with a membrane anchor that links it to the surface of CAR-iNKT cells. 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 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

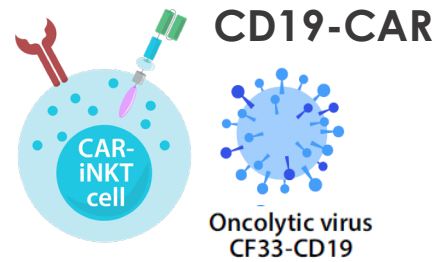
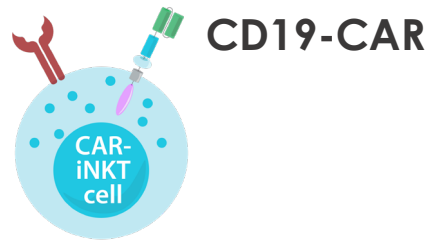
The technology has been published in the prestigious, peer reviewed journal, **Nature Communications**

[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**

# Arovella's expanding pipeline



ALA-101

ALA-101 + onCARlytics

CLDN18.2

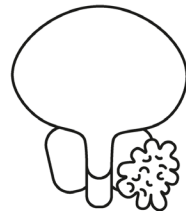
IL-12-TM



Non-Hodgkin's Lymphoma



Head and Neck Cancer



Prostate Cancer



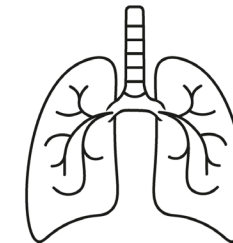
Brain Metastases



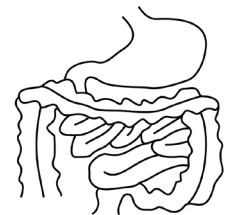
Triple negative breast cancer



Pancreatic Cancer



Lung Cancer



Gastric Cancers



# Upcoming milestones for 2024

January  
2024

July  
2024

December  
2024

## ALA-101 (CD19)

- Complete cGMP manufacture for Phase 1 clinical trials
- Complete preparatory activities for Phase 1 study, including preparation of regulatory dossier, engagement with clinical sites and KOLs

- Commence Phase 1 for ALA-101 targeting CD19+ lymphoma and leukemia

## ALA-105 (CLDN18.2)

- Initiate proof-of-concept testing for CLDN18.2-iNKT cells to expand iNKT platform for treatment of solid tumours
- Optimise 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)

## iNKT Cell Therapy Platform

- 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
- Confirm activity of ALA-101 in combination with Imugene's onCARlytics to target solid tumours in animal models



### Expect to advance ALA-101 to Phase 1 first-in-human clinical trial during 2024

Dose escalation Phase 1 study in patients with CD19+ blood cancers

# 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



## Lead product progressing to clinical trials

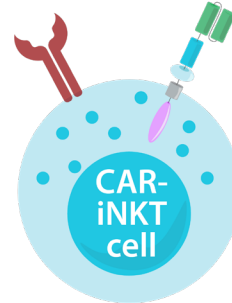
ALA-101, a potential treatment for CD19-expressing blood cancers, is being progressed to Phase 1 clinical trials, expected to commence in 2024

## Arovella has an expanding pipeline

Arovella continues to expand the iNKT cell platform to potentially treat solid tumours



# Arovella's CAR-iNKT Cell Platform



## Improved manufacturing logistics

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



## 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



## 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



ASX:ALA



# Thank You

**Dr. Michael Baker**

CEO & Managing Director

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Mobile: +61 403 468 187



# Cell therapy deal references

1. <https://www.astrazeneca.com/media-centre/press-releases/2023/astrazeneca-to-acquire-gracell-furthering-cell-therapy-ambition-across-oncology-and-autoimmune-diseases.html>
2. <https://www.astrazeneca.com/media-centre/press-releases/2023/astrazeneca-cell-and-gene-therapy-deal-w-collectis.html>
3. <https://www.businesswire.com/news/home/20230815091930/en/Precision-BioSciences-Completes-Strategic-Transaction-with-Imugene-for-Azer-Cel-in-Cancer>
4. <https://www.astellas.com/en/news/28271>
5. <https://www.jnj.com/janssen-enters-worldwide-collaboration-and-license-agreement-with-cellular-biomedicine-group-to-develop-next-generation-car-t-therapies>
6. <https://www.astrazeneca.com/media-centre/press-releases/2023/acquisition-of-neogene-therapeutics-completed.html>
7. <https://www.gilead.com/news-and-press/press-room/press-releases/2022/12/kite-and-arcellx-announce-strategic-collaboration-to-co-develop-and-co-commercialize-late-stage-clinical-cart-ddbcma-in-multiple-myeloma>
8. <https://www.fiercebiotech.com/biotech/genentech-pays-70m-access-arsenals-armoury-t-cell-tools-quest-solid-tumor-car-t>
9. <https://www.prnewswire.com/news-releases/poseida-therapeutics-announces-strategic-global-collaboration-with-roche-focused-on-allogeneic-car-t-cell-therapies-for-hematologic-malignancies-301598555.html>
10. <https://www.adaptimmune.com/investors-and-media/news-center/press-releases/detail/197/adaptimmune-enters-into-a-strategic-collaboration-with>
11. <https://www.gilead.com/news-and-press/press-room/press-releases/2021/8/kite-and-appia-bio-announce-collaboration-to-research-and-develop-allogeneic-cell-therapies-for-cancer>
12. [https://www.nasdaq.com/articles/athenex-snaps-up-kuur-therapeutics-for-\\$185m-street-sees-133.7-upside-2021-05-05](https://www.nasdaq.com/articles/athenex-snaps-up-kuur-therapeutics-for-$185m-street-sees-133.7-upside-2021-05-05)
13. <https://eternatx.com/news/brooklyn-immunotherapeutics-completes-acquisition-of-eterna-therapeutics/>