ASX Release

14 March 2024

SPARK PLUS SINGAPORE HEALTHCARE DAY PRESENTATION

Highlights:

- **Arovella presents at Spark Plus Singapore Healthcare Day**

MELBOURNE, AUSTRALIA 14 March 2024: Arovella Therapeutics Ltd (ASX: ALA), a biotechnology company focused on developing its invariant Natural Killer T (iNKT) cell therapy platform, is pleased to announce that its CEO and MD, Dr Michael Baker, will today present at the Spark Plus Singapore Healthcare Day .

Dr Baker will present key pre-clinical data for Arovella's iNKT cell therapy platform and described how Arovella's technology provides important advantages over existing T-cell therapies and has the potential to be applied to both blood cancers and solid tumours. The presentation is attached to this release and is also available on the Company's website https://www.arovella.com/news-presentations.

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. Arovella is also expanding into solid tumour treatment through its CLDN18.2-targeting technology licensed from Sparx Group. 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; **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

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[1]	$143.4 million
Shares on issue	925.1 million
52-week low / high[1]	$0.033 / $0.185
Cash Balance (Dec 31 2023)	$4.76 million

Major Shareholders

Shareholder	Ownership (%) [1]
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[1]

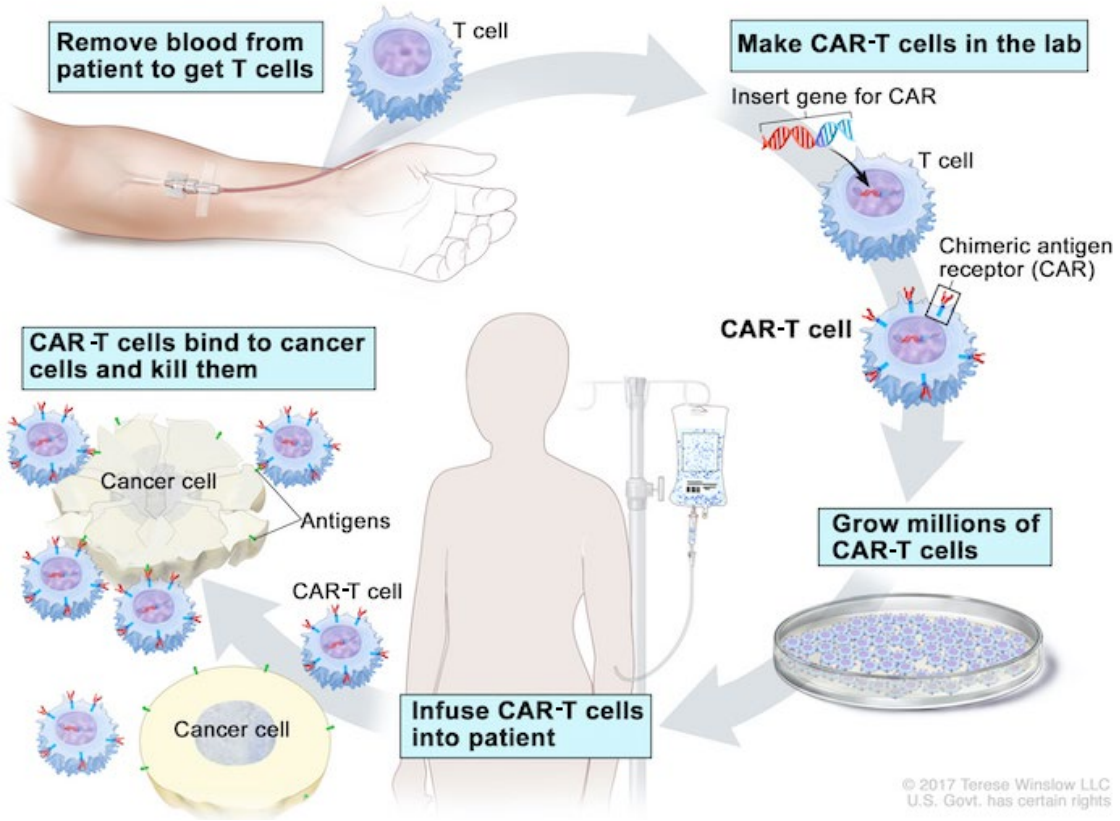
Recent cell therapy transactions[1]

Date	Type of deal	Acquirer/Licensee	Target/Licensor	Cell Type	Stage	Upfront (US$M)	Milestones (US$M)	Total deal value (US$M)
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	AthenaX	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.

https://www.ohsu.edu/sites/default/files/2021-04/CAR%20TcellTherapy7-700px.jpg

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[1]

Cure

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

Strong Sales

40-60%

Patients relapse post-CAR-T therapy[2]

Product	Approval Year	2023 Revenue
YESCARTA (axicabtagene ciloleucel)	2017	US$1498m[3]
KYMRIAH (tisagenlecleucel)	2017	US$509m[4]
Abecma (idecabtagene vicleucel)	2021	US$472m[5]

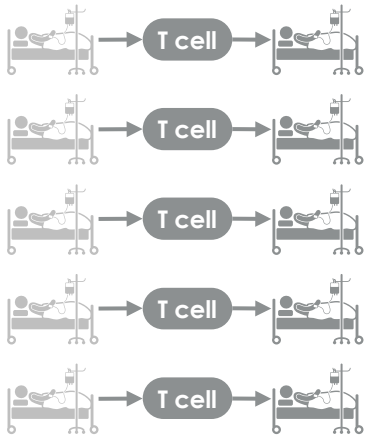
1. *https://www.businesswire.com/news/home/20230529005130/en/Global-Cell-Therapy-Market-Report-2023-Advancements-in-Biotechnology-Drives-Growth---ResearchAndMarkets.com*
2. *Zinzi et al., 2023 Pharmacological Research - 10.1016/j.phrs.2023.106742*
3. *https://www.gilead.com/news-and-press/press-room/press-releases/2024/2/gilead-sciences-announces-fourth-quarter-and-full-year-2023-financial-results#:~:text=Yescarta%C2%AE%20(axicabtagene%20ciloleucel)%20sales,%E2%80%9D)%20outside%20the%20United%20States.*
4. *https://www.novartis.com/sites/novartis_com/files/2024-01-interim-financial-report-en.pdf*
5. *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



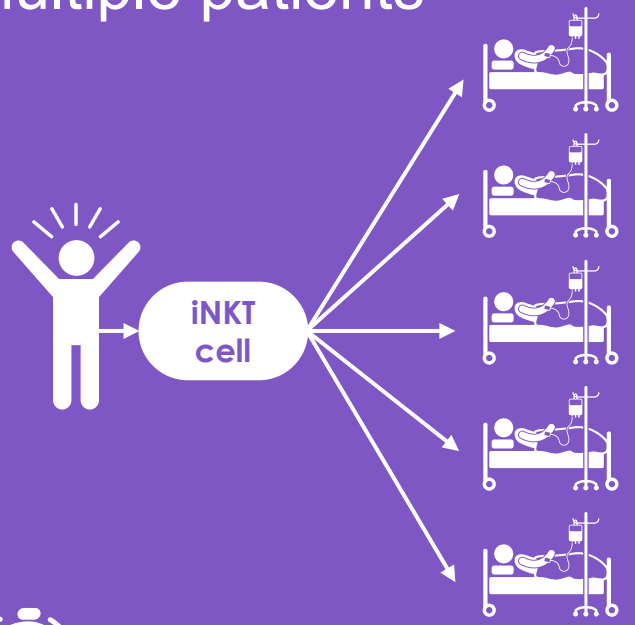
Each manufacturing batch is **patient-specific**

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

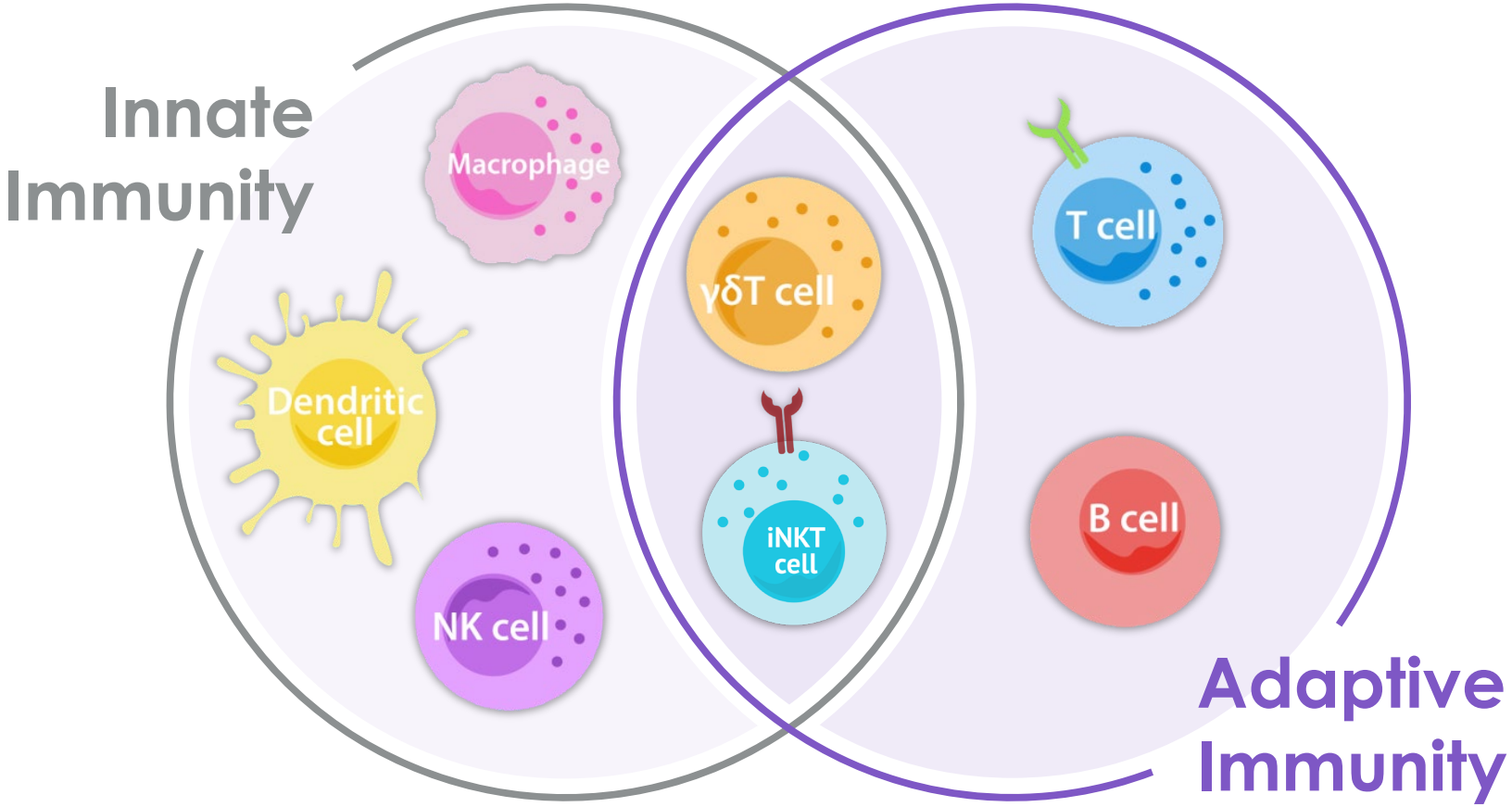


1 week

Patients ready to dose within 1 week

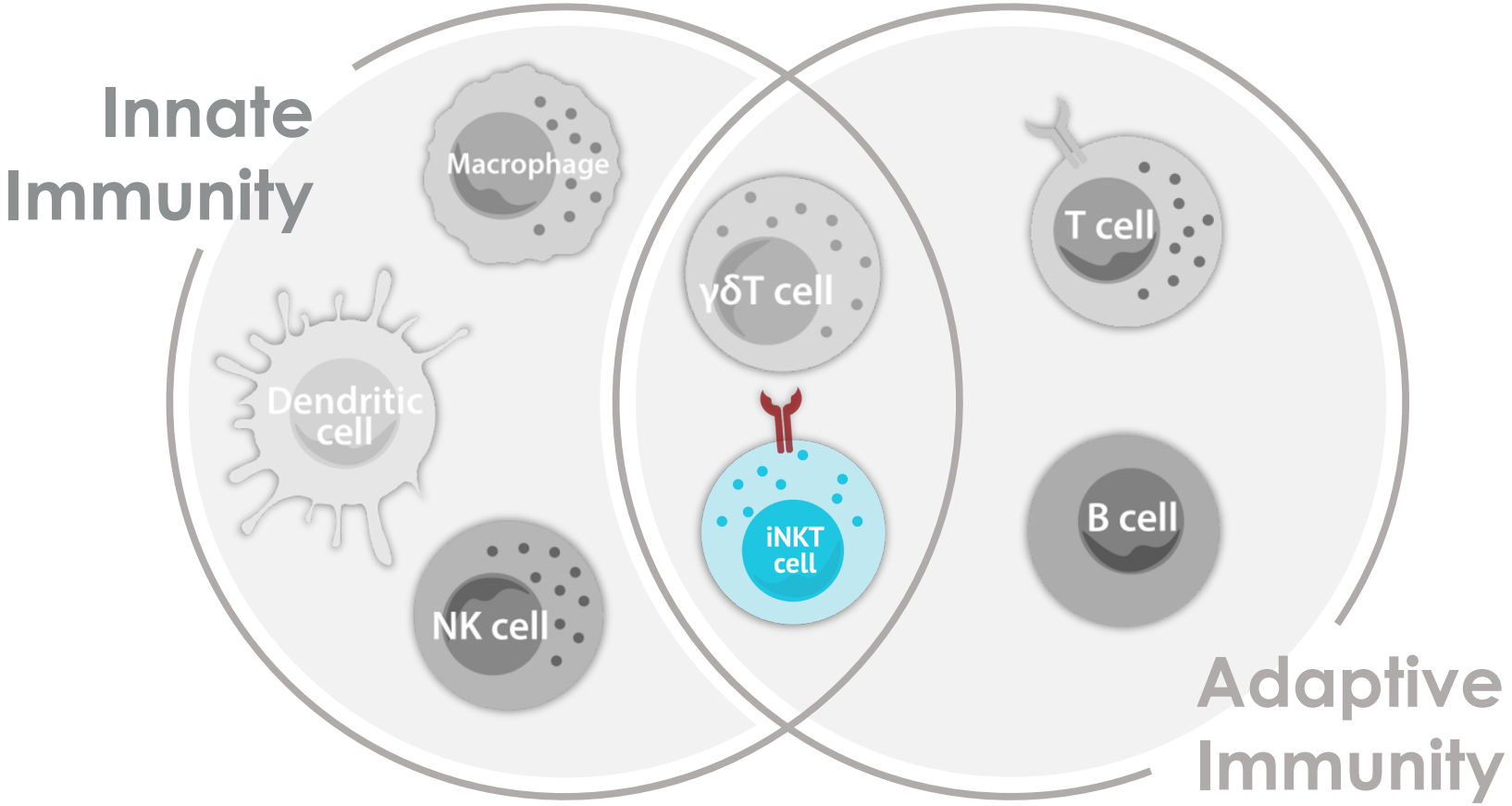
Introducing invariant Natural Killer T (iNKT) cells

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

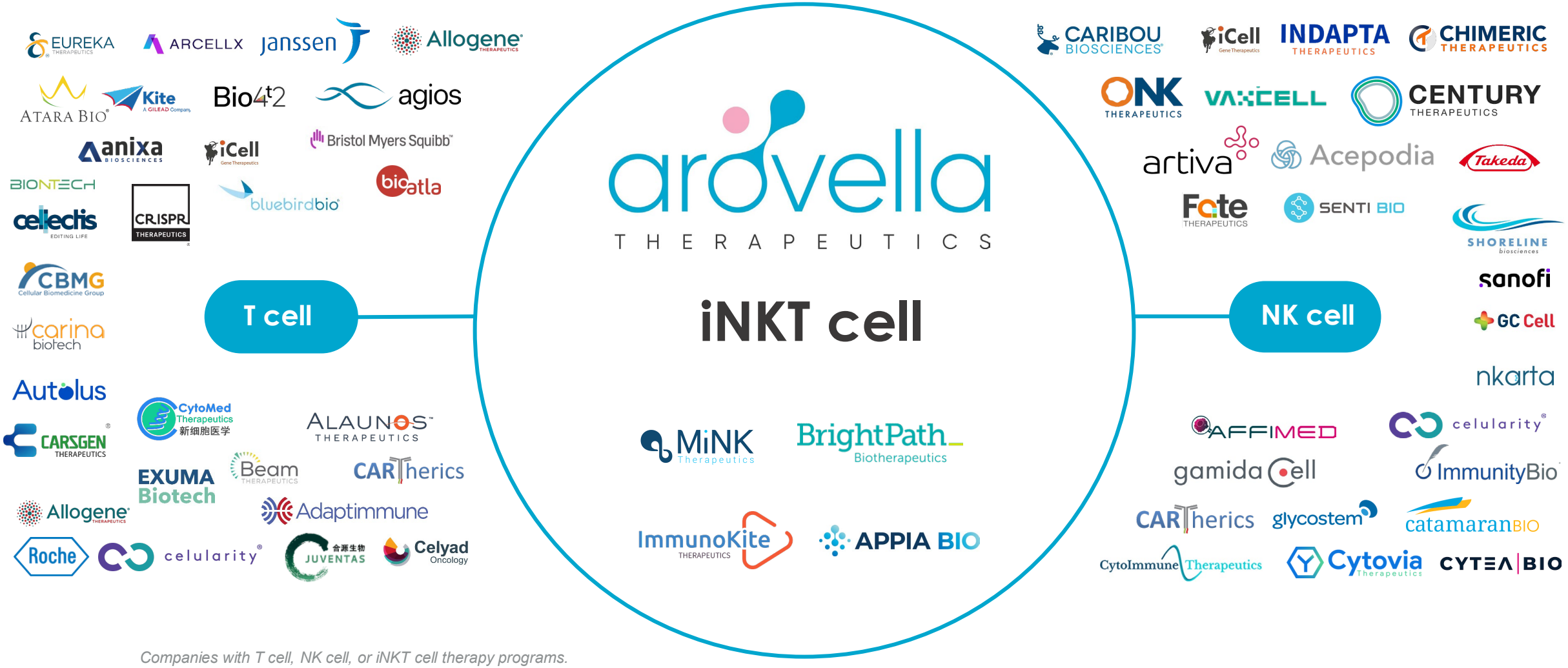
- Bridge innate & adaptive immune responses
- Contain both T cell & NK cell killing mechanisms
- Naturally target & kill cancers that express CD1d

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

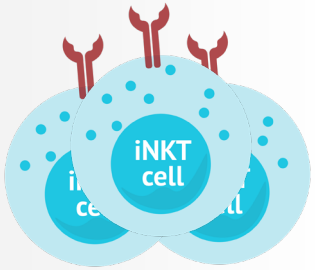
CAR-iNKT cell therapy production advantages

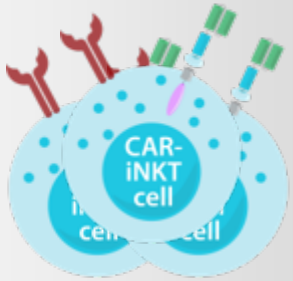
Off-the-shelf manufacturing advantages

MANUFACTURING

Collect Healthy Donor Blood

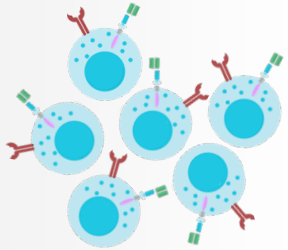
Isolate iNKT cells





Engineer iNKT cells to produce a CAR

Expand to grow billions of CAR-iNKT cells

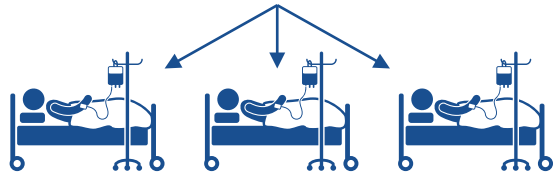


Vial and freeze CAR-iNKT cells

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

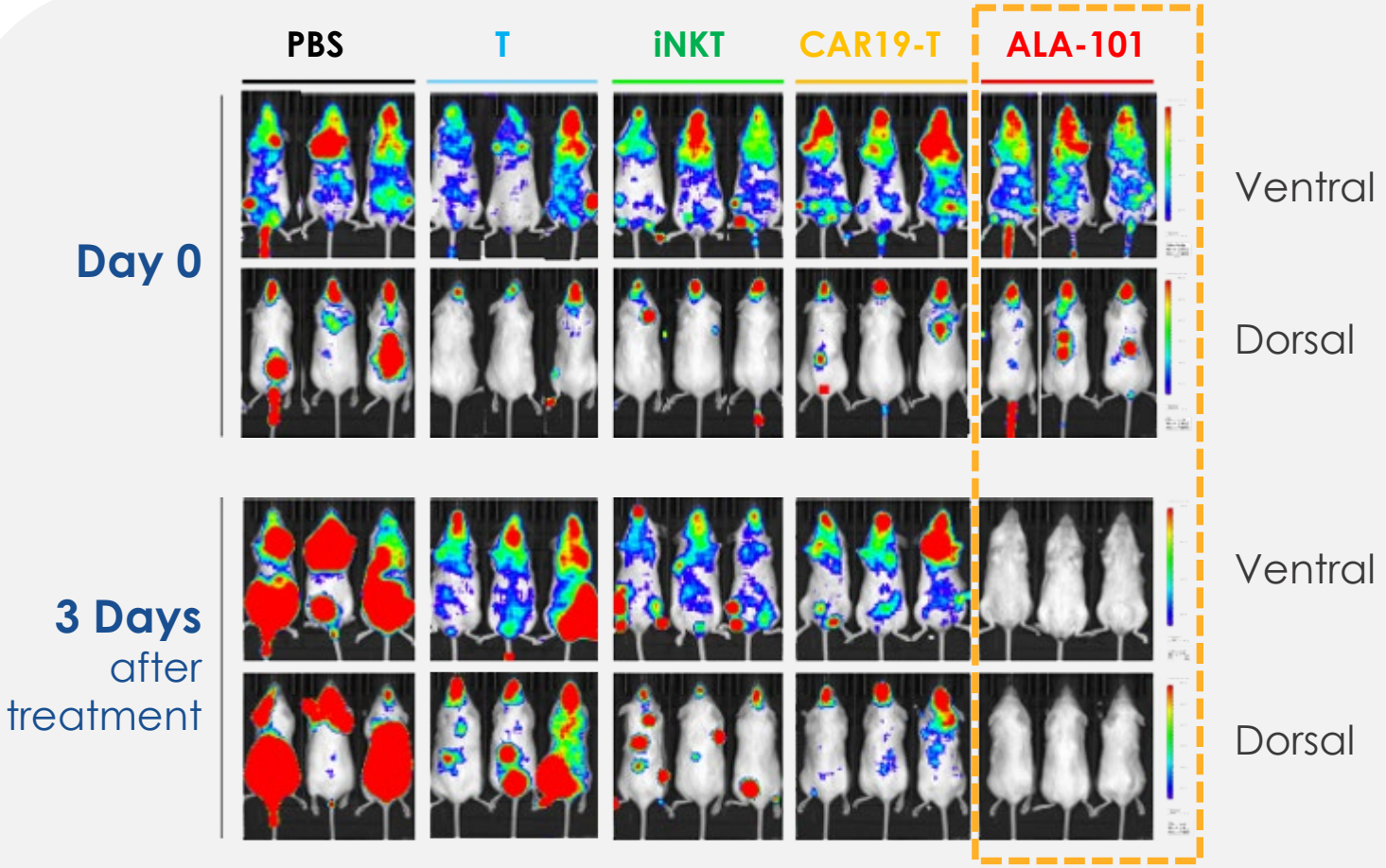
ALA-101 (CAR19-iNKT cells)

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

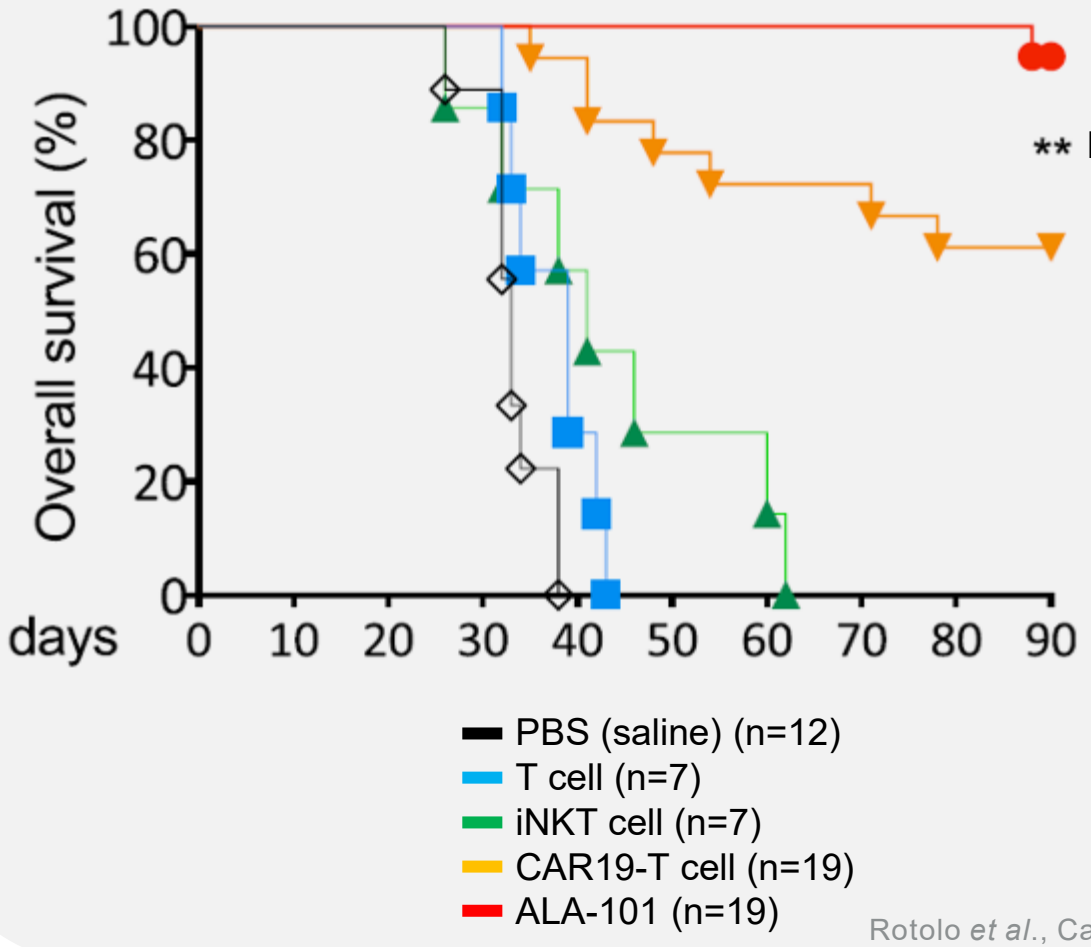


Rotolo *et al.*, Cancer Cell (2018)

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

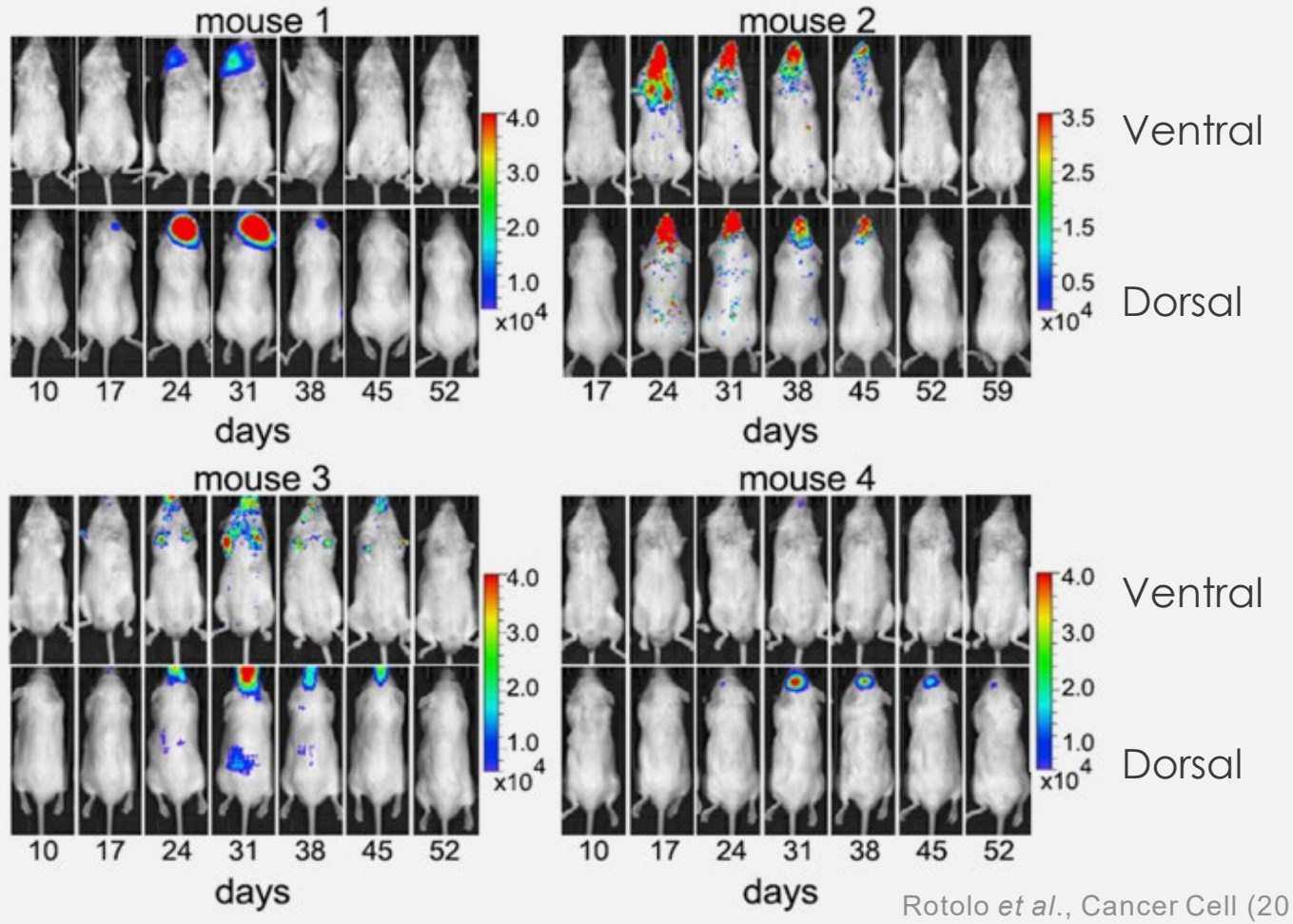


Rotolo *et al.*, Cancer Cell (2018)

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)

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.

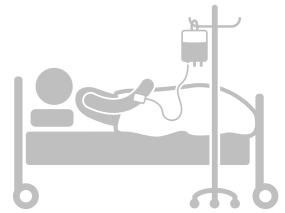
Expected to be safe

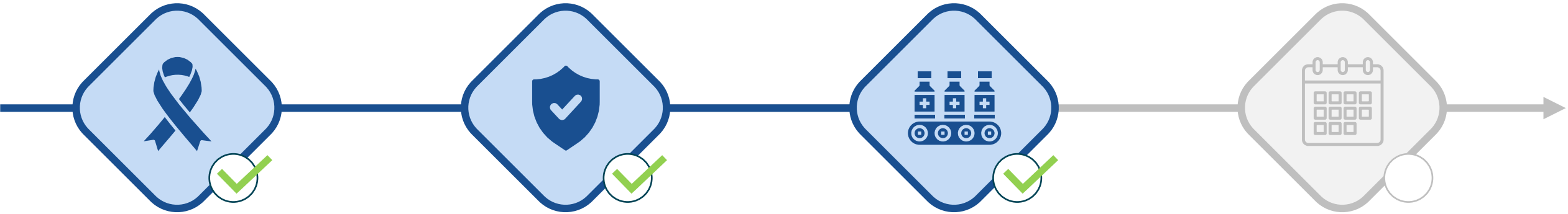
iNKT cells have been shown in clinical trials not to cause graft versus host disease (GvHD) and the CD19 targeting CAR (FMC63) is a validated targeting agent in approved cell therapies.

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[1]

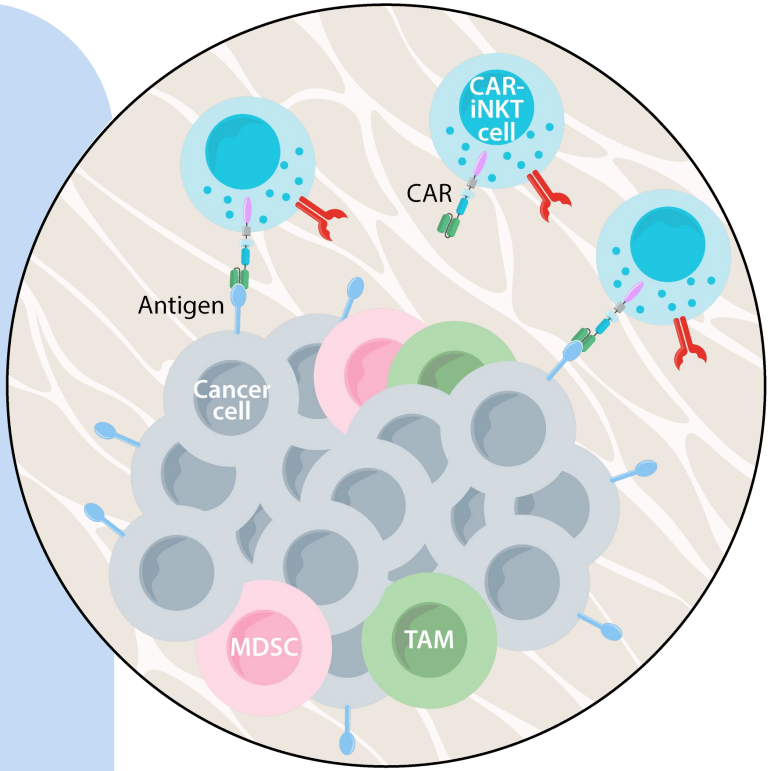
1. *https://www.cancer.gov/types/common-cancers*

Solid tumours pose challenges to cell therapies

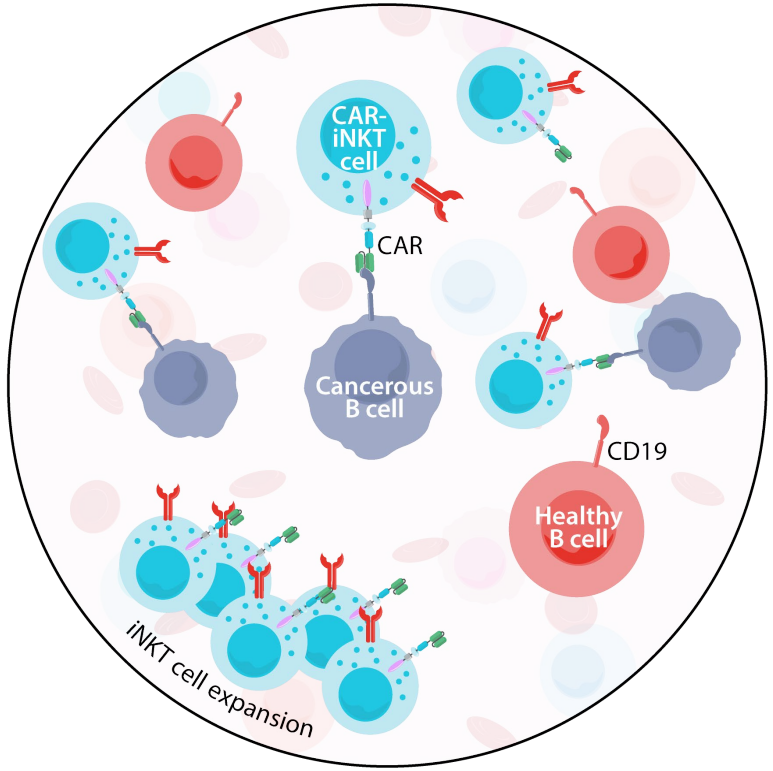
Solid tumours are more

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

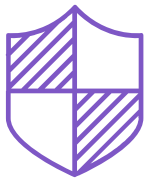
TAM = Tumour Associated Macrophage; MDSC = Myeloid Derived Suppressor Cell; CAR = Chimeric Antigen Receptor

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

STRATEGY 1

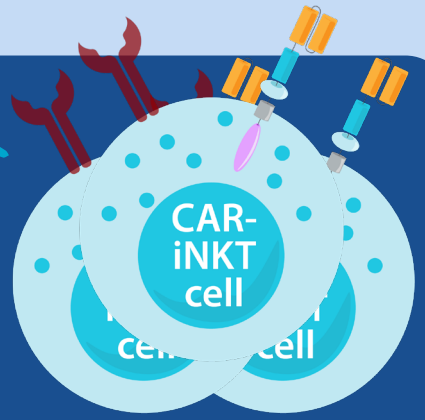
Arovella's manufacturing process can be leveraged for multiple cancer types

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

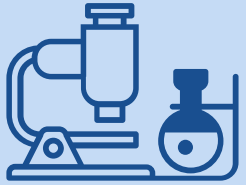
Introducing Claudin 18.2 (CLDN18.2)

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[1]

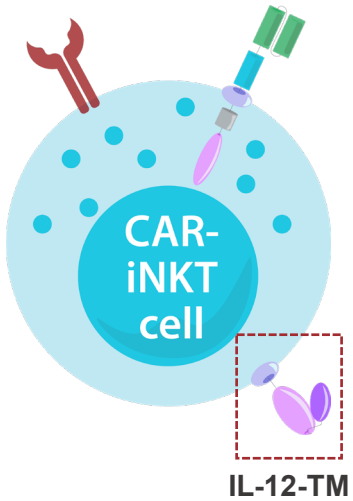
1. https://www.alliedmarketresearch.com/gastric-cancer-market-A74458#:~:text=The%20global%20gastric%20cancer%20market,cells%20lining%20of%20the%20stomach

“Armouring” CAR-iNKT cells

STRATEGY 2

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 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

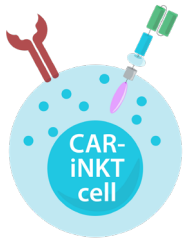
The technology has been published in the prestigious, peer reviewed journal, **Nature Communications**

nature › nature communications › articles › article

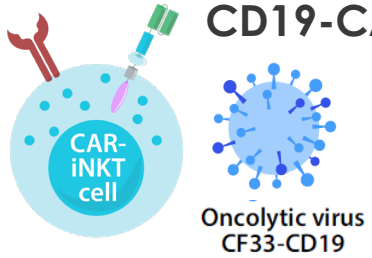
Article | Open access | Published: 02 January 2024

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

Arovella's expanding pipeline



CD19-CAR



CD19-CAR

Novel Targets

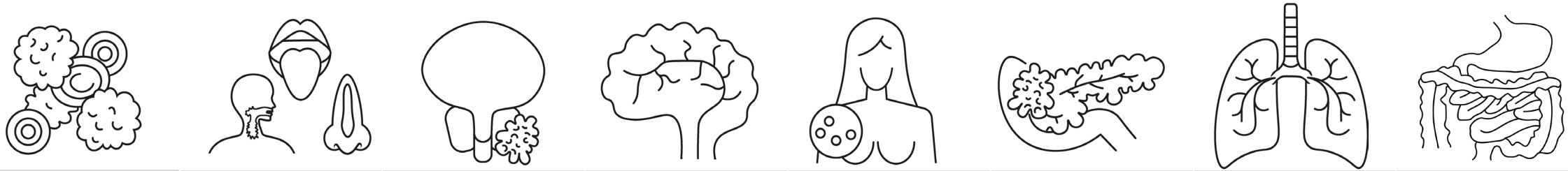
Introduction of CLDN18.2

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

cGMP – Current Good Manufacturing Practice; KOLs – key opinion leaders

Summary

Novel allogeneic CAR-iNKT cell platform

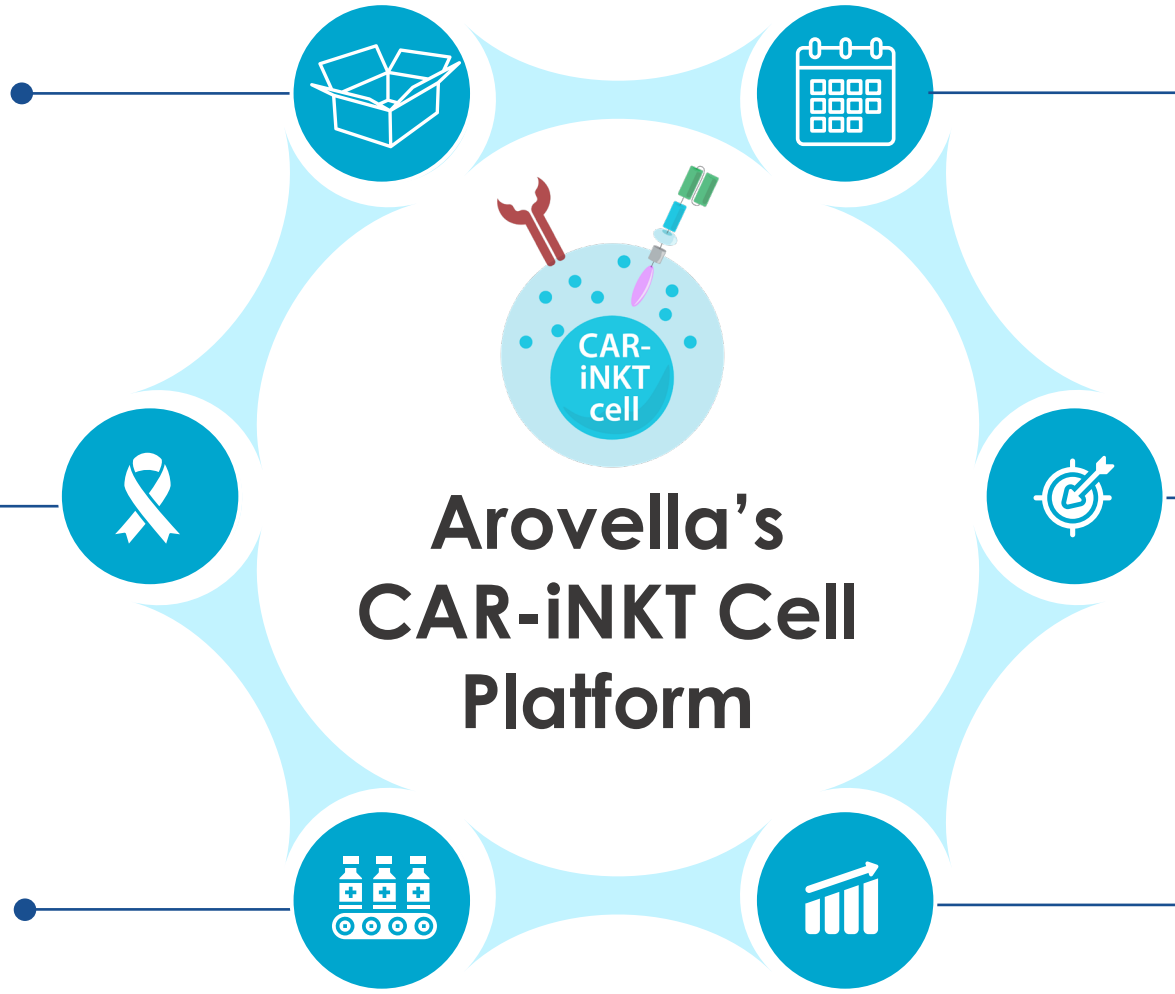
iNKT cells serve as an excellent platform to develop allogeneic, or “off-the-shelf”, cell therapies to treat cancer

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 2024

Arovella has an expanding pipeline

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

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

ASX:**ALA**

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THERAPEUTICS

Thank You

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