ASX Release

22 June 2023

AROVELLA INVESTOR WEBINAR PRESENTATION

- **Investor webinar to be held at 11 AM AEST today**
- **Discussing next steps for Arovella and its opportunity in developing the iNKT cell platform**

MELBOURNE, AUSTRALIA 22 June 2023: Arovella Therapeutics Ltd (ASX: ALA) is pleased to provide the presentation to be delivered at its webinar scheduled for today at 11:00 AM (AEST).

Following the Company's recent capital raising, the webinar will discuss the next steps for Arovella and its opportunities in developing the iNKT cell platform.

Presenting on the webinar will be CEO and MD Dr Michael Baker.

Details of the Investor Webinar are below:

Time: **11:00 AM (AEST)**

Date: **Today, Thursday, the 22nd of June 2023**.

Registration: **https://us02web.zoom.us/webinar/register/WN_D86Vu_gkR6CbU11IjJgHCg**

Further details on how to attend will be provided by email following registration.

A webinar recording will be made available via the Company's website and social media channels following the event.

Questions can be submitted during the webinar or sent in advance to investor@arovella.com.

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
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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 is also expanding its DKK1-peptide targeting technology licenced from MD Anderson and used in conjunction with its 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. For more information, visit www.arovella.com

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.

The Company is also commercialising ZolpiMist™ to treat short-term insomnia.

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 actions of third parties and financial terms. These factors and assumptions are based upon currently available information and the forward-looking statements contained herein speak only as 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; 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.

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THERAPEUTICS

ASX:ALA

Investor Webinar
June 2023

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Arovella Therapeutics Highlights

Off-the-Shelf iNKT Cell Platform

Arovella is 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 being progressed to phase I clinical trials, expected to commence in 2024

Addressing Key Unmet Need

Arovella's iNKT cell platform is well positioned to solve key challenges that hamper the cell therapy sector

Strong Leadership Group

Arovella's leadership team and its Board have proven experience in drug development, particularly cell therapies

Strategic Acquisitions

Arovella is focused on acquiring innovative technologies that strengthen its cell therapy platform and align with its focus areas

Unique Value Proposition

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

Arovella Financial Overview

Financial Snapshot

ASX CODE	ALA
Market capitalisation[1]	$42.5 million
Shares on issue	849.9 million
52-week low / high[1]	$0.020 / $0.105
Pro Forma Cash (March 31, 2023)[2]	$7.1 million

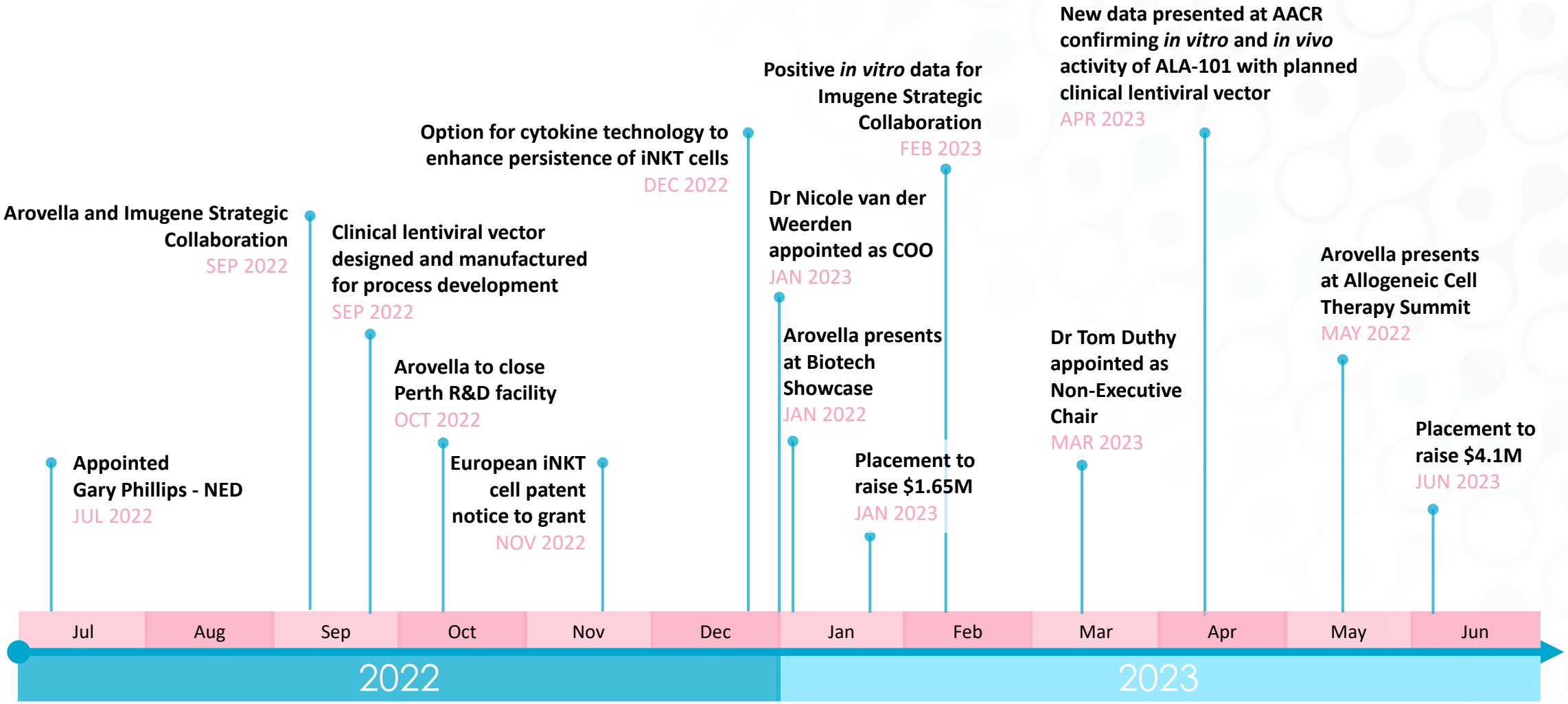
Major Shareholders

Shareholder	Ownership (%)[1]
MERCHANT FUNDS MANAGEMENT PTY LTD	86,210,282 (11.36%)
RICHARD JOHN MANN	54,458,288 (6.40%)
UBS NOMINEES PTY LTD	20,620,196 (2.45%)
BLACKBURNE CAPITAL PTY LTD	18,250,000 (2.17%)
DYLIDE PTY LTD	15,000,000 (1.78%)

- Share Purchase Plan currently underway to raise an additional $1m

1. *As of 20 June 2023*
2. *Includes the proceeds from the Placement announced 7 June 2023, net of transaction costs*

Recent Milestones



Recent Cell Therapy Transactions

Date	Type of deal	Acquirer/Licensee	Target/Licensor	Stage	Upfront ($M)	Milestones ($M)	Total deal value ($M)
May-23	License	janssen	CBMG Cellular Biomedicine Group	Phase Ib	$245	undisclosed	
Jan-23	Acquisition	AstraZeneca	neogene THERAPEUTICS	Phase I	$200	$120	$320
Oct-22	Development collaboration	GILEAD	ARCELLX	Phase II	$225*	undisclosed	
Sep-22	Research collaboration	Genentech A Member of the Roche Group	ArsenalBio™	Preclinical	$70	undisclosed	
Aug-22	Licence and strategic collaboration	Roche	POSEIDA THERAPEUTICS	Phase I	$110	$110	$220
Sep-21	Development collaboration	Genentech A Member of the Roche Group	Adaptimmune	Preclinical	$150	$150	$300
Aug-21	Research collaboration	GILEAD	APPIA BIO	Preclinical	undisclosed	undisclosed	$875
May-21	Acquisition	Athenex	kuur THERAPEUTICS	Phase I	$70	$115	$185
Jun-21	Acquisition	eterna	Novellus THERAPEUTICS	Preclinical	$125	$0	$125
Dec-19	Acquisition	astellas	XYPHOS	Preclinical	$120	$545	$665
				Mean	**$146**	**$208**	**$364**

Arcellx also received a $100m equity investment from Gilead

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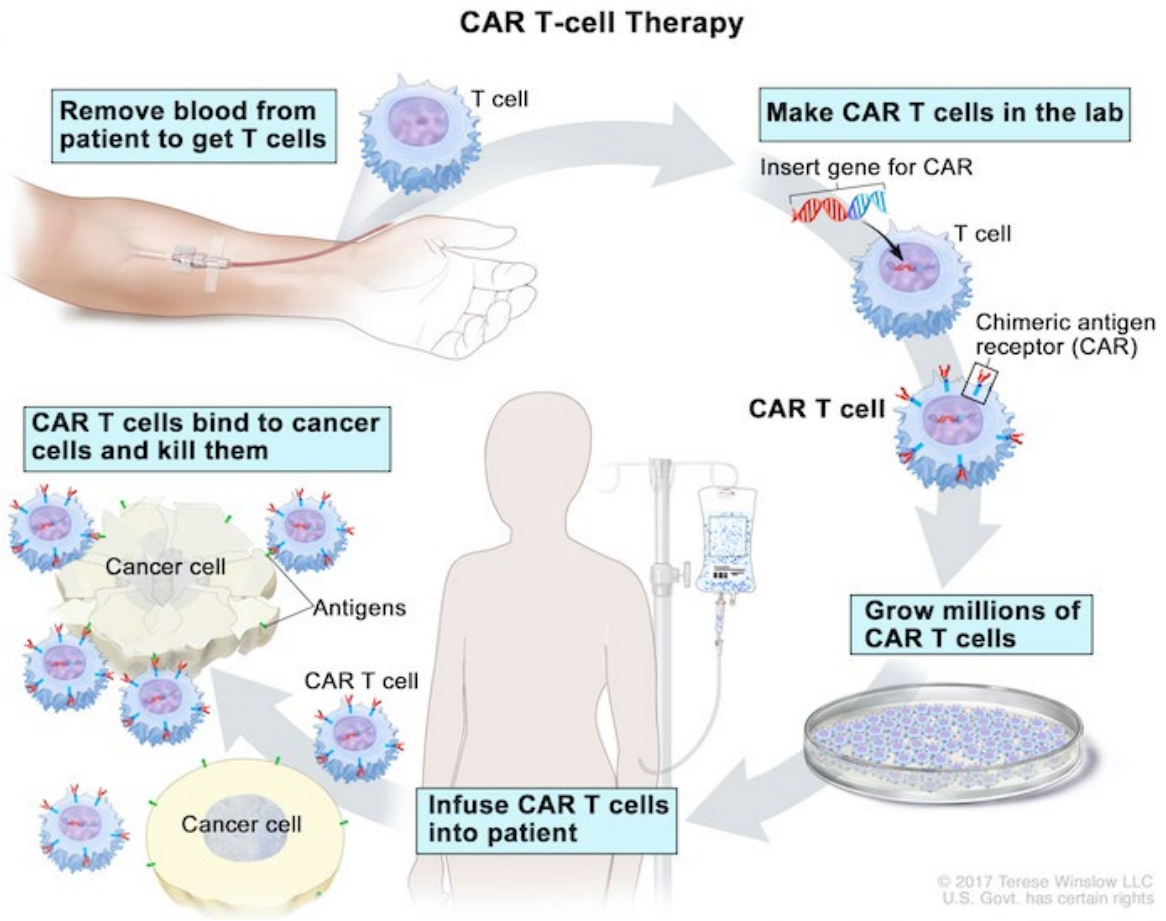
What are "CAR-T Cells"?

- T cells are a common type of immune cell that fight infections and can help fight cancer
- 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 is able to specifically recognise cancer cells through a target antigen
- 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

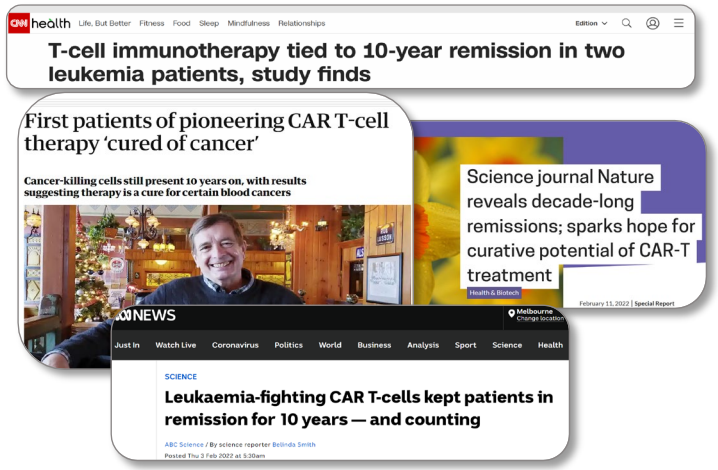


https://www.ohsu.edu/sites/default/files/2021-04/CAR%20TcellTherapy7-700px.jpg

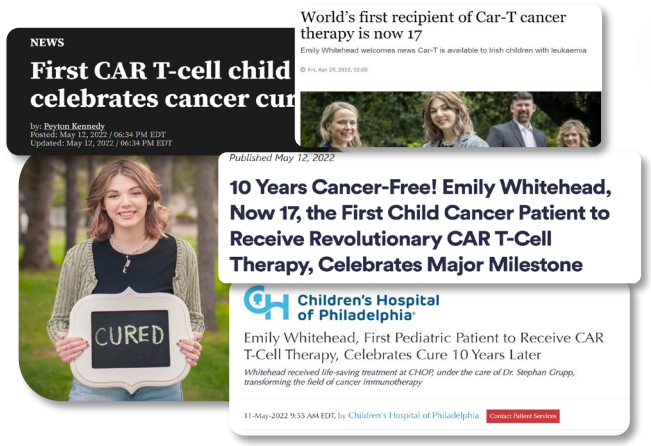
Cell Therapy Has Revolutionized Blood Cancer Treatment

- CAR-T cells have demonstrated ability to **cure** haematological cancers and have generated strong sales
- The Cell Therapy market is expected to reach $61.2 billion by 2030[1]

February 2022



May 2022



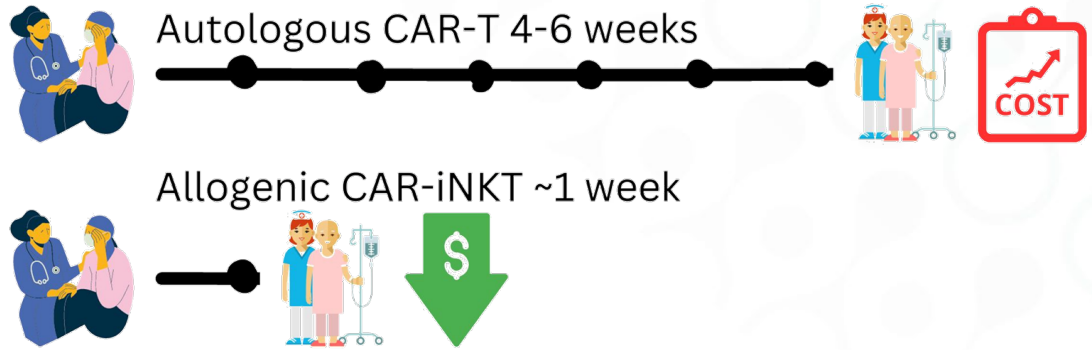
Product	Approval Year	2022 Revenue
YESCARTA® (axicabtagene ciloleucel)	2017	US$1160m[2]
KYMRIAH® (tisagenlecleucel)	2017	US$536m[3]
Abecma® (idecabtagene vicleucel)	2021	US$388m[4]

1. *https://www.businesswire.com/news/home/20230529005130/en/Global-Cell-Therapy-Market-Report-2023-Advancements-in-Biotechnology-Drives-Growth---ResearchAndMarkets.com*
2. *https://s29.q4cdn.com/585078350/files/doc_financials/2022/q4/GILD-Q4-FY22-Earnings-Press-Release-2-February-2023.pdf*
3. *https://www.novartis.com/sites/novartis_com/files/q4-2022-media-release-en.pdf*
4. *https://bioprocessintl.com/bioprocess-insider/therapeutic-class/bms-sees-car-t-sales-rocket-in-line-with-increased-capacity/#:~:text=For%20the%20full%20year%202022,%2487%20million%20the%20year%20prior.*

But…Manufacturing and Logistics Pose Major Challenges

- **T cells must originate from the patient to be treated** so each manufacturing batch is patient-specific
  - **High manufacturing and supply chain costs** lead to high drug costs (>$500k per patient)
  - Starting material (T cells) can be compromised due to disease, **reducing efficacy**
  - Limited number of centres able to collect cells and manufacture the therapy so **not all eligible patients can be treated**
- **Manufacturing CAR-T takes 4-6 weeks** for each patient
  - Patients with aggressive disease sometimes **die while waiting for treatment**
  - **Manufacturing run failures can occur**, further increasing the time to treatment (and cost)

Arovella's allogeneic CAR-iNKT cell platform has the potential to address the manufacturing and logistics challenges of CAR-T cells and the potential for improved efficacy



Advantages of iNKT Cells

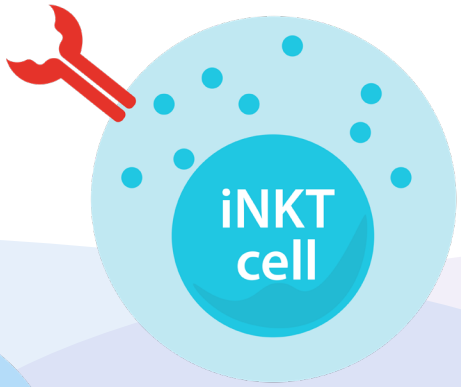
Cells from a healthy donor can be used to treat patients (no GvHD)

Naturally target tumour cells through invariant TCR (CD1d); **dual targeting with CAR**

Directly kill tumour cells via T-cell and NK-cell-like mechanisms

iNKT cells

subpopulation of T cells with properties of NK cells



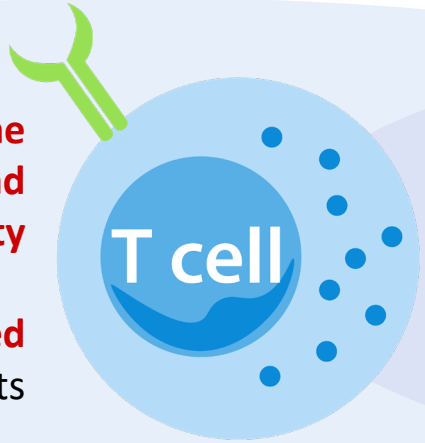
Modify the tumour microenvironment and **kill cells that promote tumour growth**

Infiltrate tumours and once activated, secrete signaling molecules to **activate other immune cells** to kill tumour cells

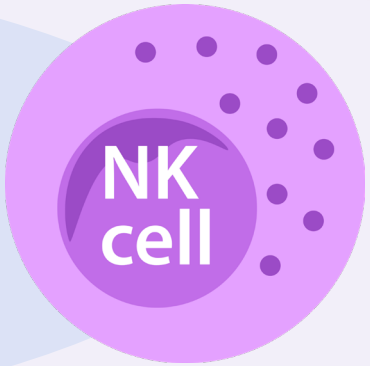
ADAPTIVE IMMUNITY

Can cause **severe cytokine release syndrome and neurotoxicity**

Complex gene editing required for allogeneic products



INNATE IMMUNITY



Limited persistence in an allogeneic setting

Limited durability of response

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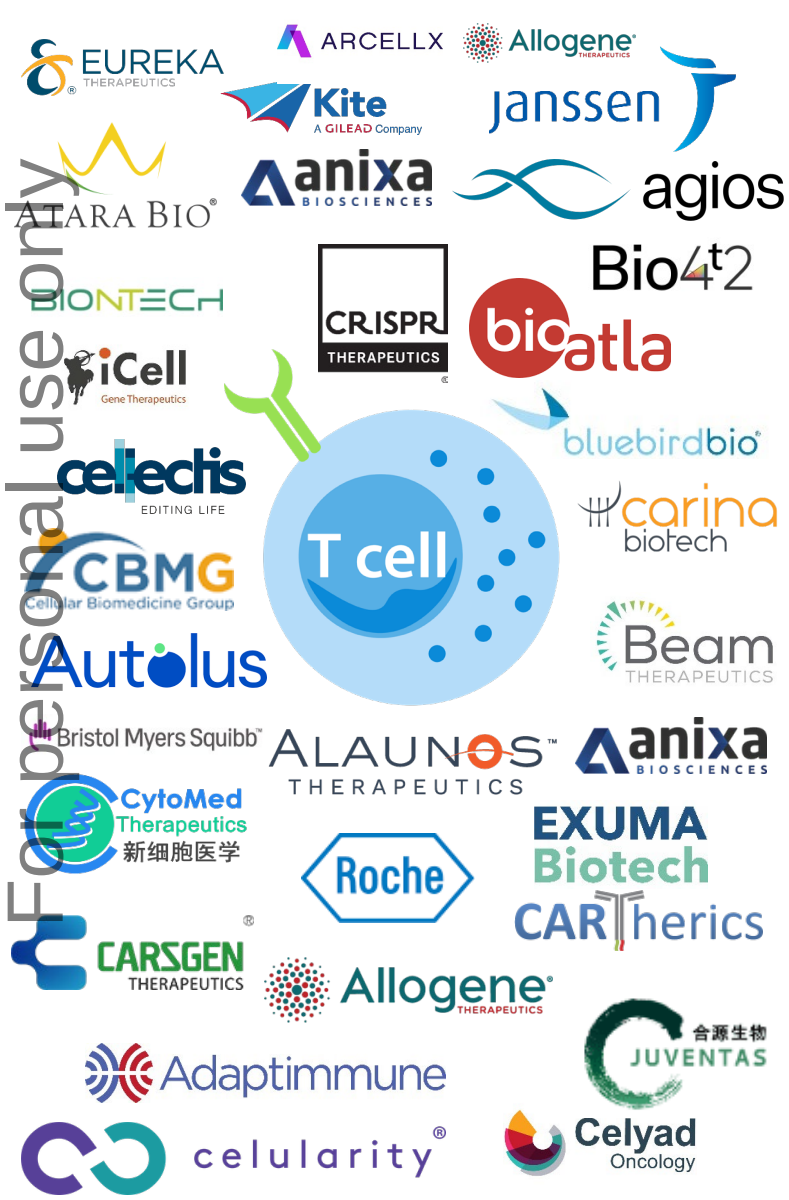
The Potential of CAR-iNKT Cells is Untapped



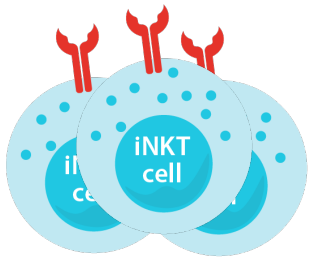
Companies with T cell, NK cell, or iNKT cell therapy programs. Source: Company analysis based on public information

CAR-iNKT Cell Therapy Production Advantages

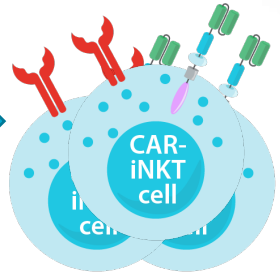
MANUFACTURING

Collect Healthy Donor Blood

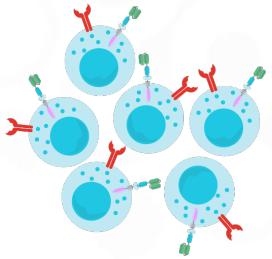
Isolate iNKT cells



Engineer iNKT cells to produce a CAR



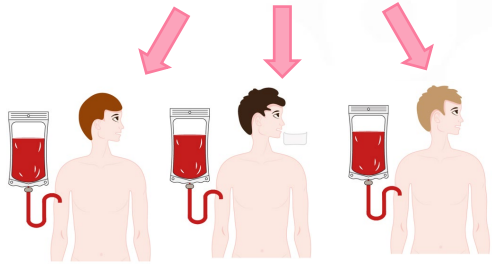
Expand to grow billions of CAR-iNKT cells



Vial and freeze CAR-iNKT cells

Thaw CAR-iNKT cells

Dose eligible patients



TREATMENT

Allogeneic Manufacturing Advantages

1. Healthier starting material
   - Potentially better efficacy
2. Scalable manufacturing with reduced costs
   - Reach more patients
3. Faster access to treatment
   - Improved outcomes for aggressive cancers
4. Removes risk of manufacturing run failure

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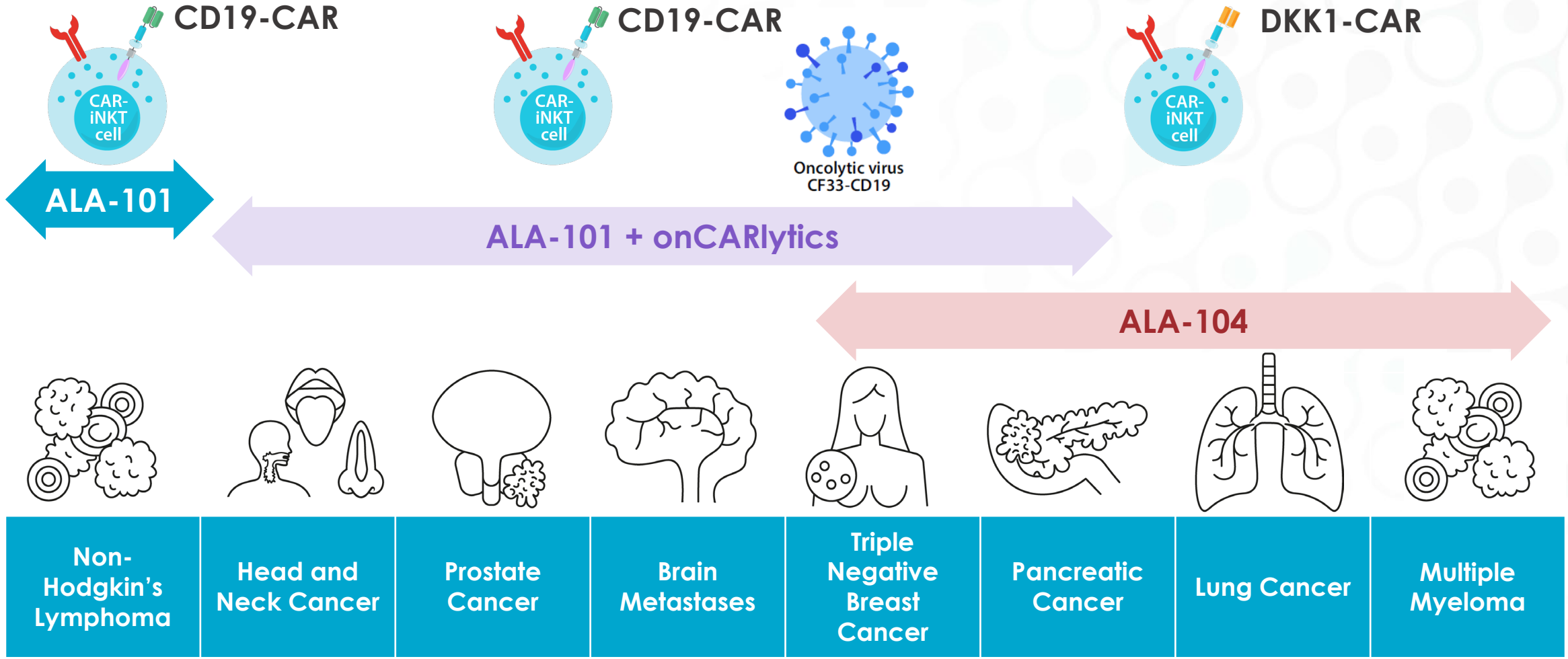
Arovella's Potential Cancer Targets



- Additional CARs can be used to target different cancer types:
  - **Blood Cancers** - CD20, CD22, CD79b; **Solid tumours** – mesothelin, EGFRvIII, IL13α32, GPC3, HEPG2, GD2

CAR19-iNKT (**ALA-101**)

An off-the-shelf cell therapy for CD19-expressing cancers

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CD19-expressing Blood Cancers

Incidence

- CD19 is commonly expressed on B cell blood cells, including:
- **B cell Non-Hodgkin's Lymphomas**
  Annual incidence of ~65,000 in the US[1] and ~95,000 in Europe[2]
- More than 60% of patients do not achieve long-term remission with first-line approved therapies
- **B cell Leukaemias**
  Annual incidence of ~23,000 in the US (~5,500 deaths)[1]

Current Treatments

- Four approved autologous CAR-T products target CD19
- **Autologous CAR-T recently elevated to 2nd-line therapy**
- 6-month complete response rates for auto-CAR-T in relapsed and refractory DLBCL is only 30-35%
- Substantial safety risk with high rates of CRS, ICANS and infection
- **Significant unmet need remains**

ALA-101 solution

- ALA-101 is an off-the-shelf iNKT cell therapy that targets CD19-expressing cancer cells
- **ALA-101 is an attractive potential treatment for B cell Lymphomas and Leukaemias**
- Phase I clinical trial in Non-Hodgkin's lymphoma expected to commence in 2024

NHL = Non-Hodgkin's Lymphoma; DLBCL =Diffuse Large B Cell Lymphoma; CRS = Cytokine Release Syndrome; ICANS = Immune Effector Cell Associated Neurotoxicity Syndrome

1. American Cancer Society, Cancer Facts and Figures 2023, 2. IHE, Comparator Report on Cancer in Europe 2019, 3. https://www.targetedonc.com/view/epidemiology-in-b-cell-malignancies

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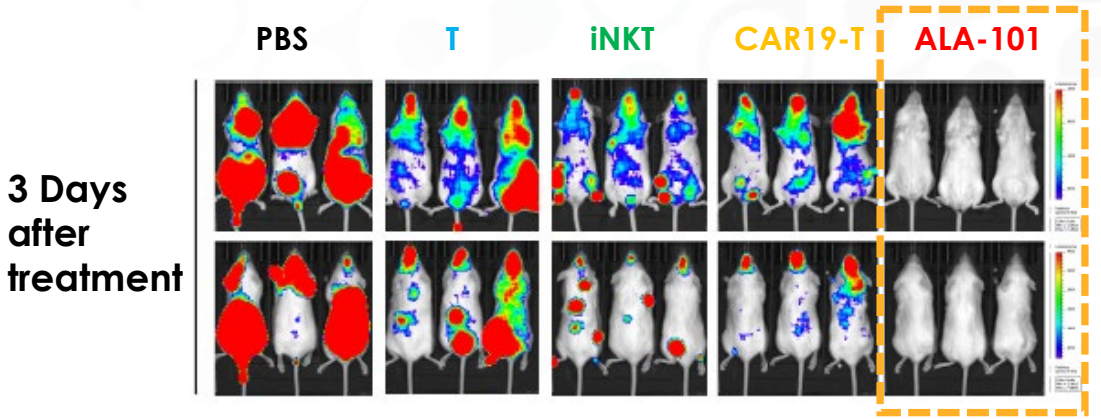
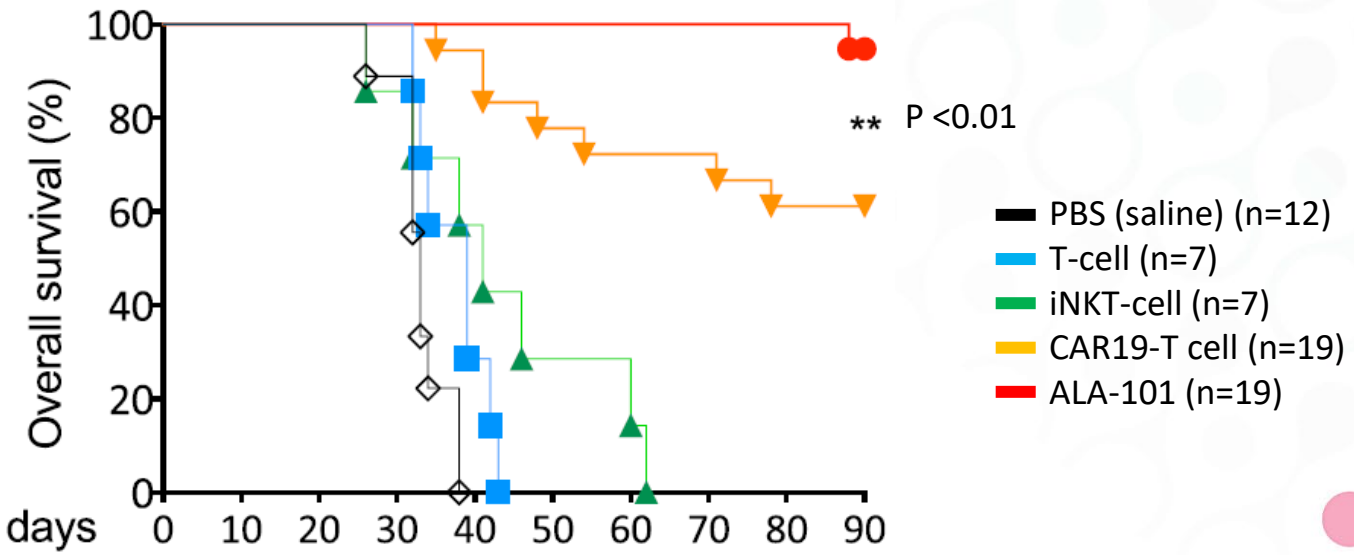
ALA-101: Superior Activity Over CAR-T Cells

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
- 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**



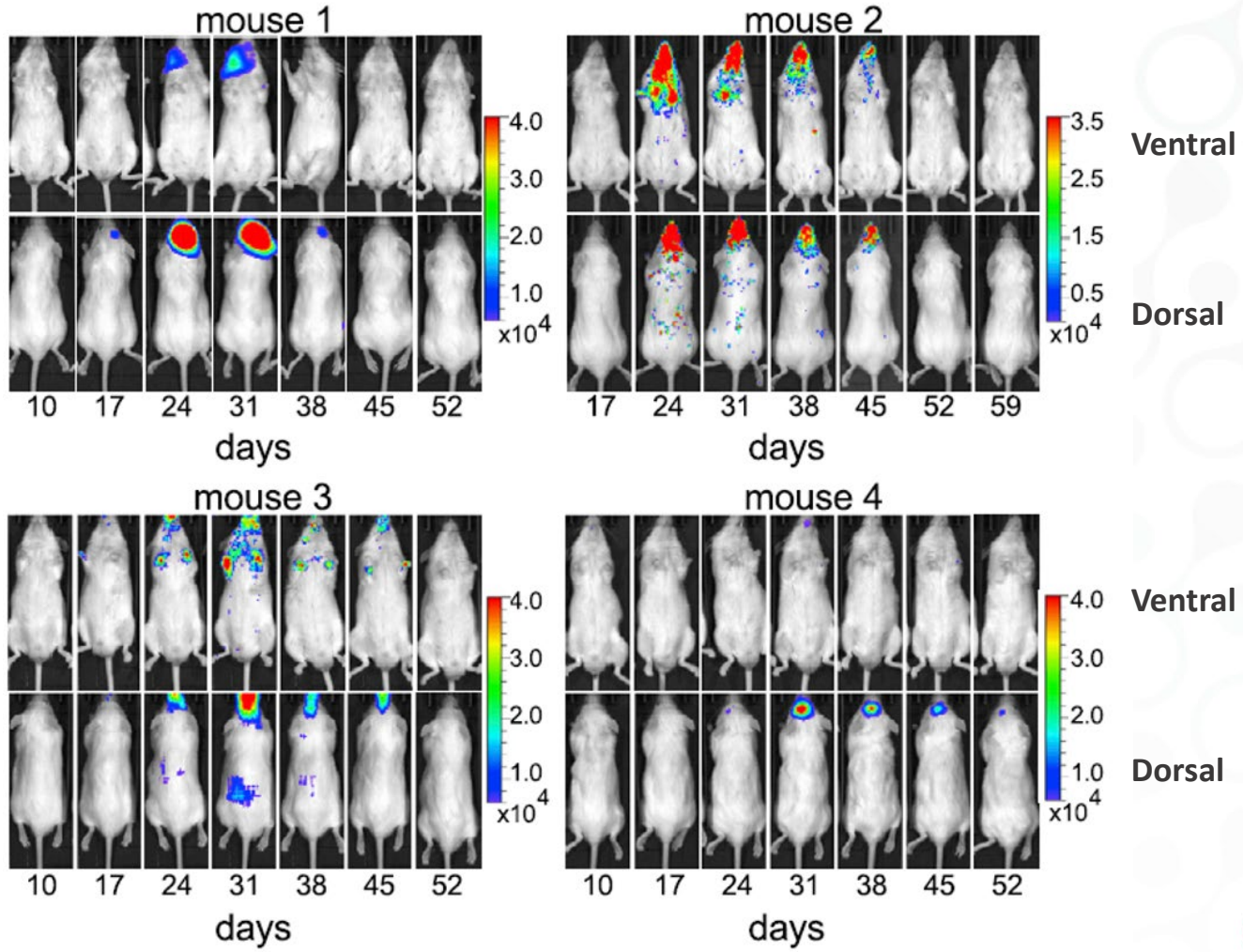


Rotolo *et al.*, Cancer Cell (2018)

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 ALA-101 (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)

New Data Presented at AACR 2023

Key Highlights:

- iNKT cells could be **well expanded**
- Following expansion, ALA-101 cells **retained the ability to multiply further when exposed to tumour cells** that express CD19
- Once stimulated, ALA-101 cells **express anti-cancer cytokines**
- ALA-101 **killed tumour cells that express CD19**, including primary patient tumour cells
- ALA-101 **significantly extended the lifespan of mice** with aggressive human B-Cell Acute Lymphoblastic Leukemia (B-ALL) that does not express CD1d

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ALA-101 Overview

- Arovella's proprietary manufacturing process allows for efficient expansion of iNKT cells while retaining functionality
  - *Essential to produce multiple doses from a single batch and address the manufacturing costs and logistical challenges of current autologous therapies*

- Arovella has produced ALA-101 using a 3rd-generation lentiviral vector in preparation for the manufacture of clinical material
  - *Lentiviral vector and genetic elements with a proven safety profile*

- ALA-101 conferred significant anti-tumour effect and significantly extended lifespan in an aggressive model of human B-Cell Acute Lymphoblastic Leukemia (B-ALL)
  - *Confirming the potential of ALA-101 as an effective treatment for CD19+ leukemias and lymphomas*

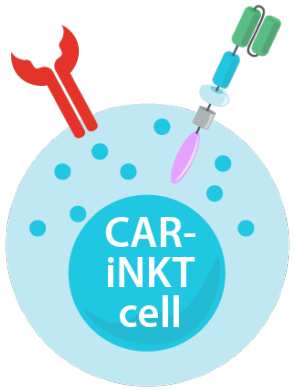
Arovella continues to progress ALA-101 towards first-in-human clinical trials

ALA-101 + CF33-CD19

An off-the-shelf cell therapy and oncolytic virus combination to mark and destroy solid tumours

Combining ALA-101 and CF33-CD19 (onCARlytics)

- ALA-101 is very potent and is rapidly activated to kill CD19 expressing cancers[1]
- The product is being developed as an off-the-shelf product for cancer treatment



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Imperial College London

- CF33 is an oncolytic virus that targets tumour cells[2]
- CF33 has been engineered to induce CD19 expression after tumour cells have been infected – onCARlytics[3]
- Phase 1 trials for CF33 commenced October 2021 with CHECKvacc and May 2022 with VAXINIA
- FDA cleared IND for onCARlytics and Blincyto combination study in May 2023

Oncolytic virus
CF33-CD19

IMUGENE
Developing Cancer Immunotherapies

City of Hope

1. *https://pubmed.ncbi.nlm.nih.gov/30300581/*
2. *https://pubmed.ncbi.nlm.nih.gov/32032721/*
3. *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9126033/*

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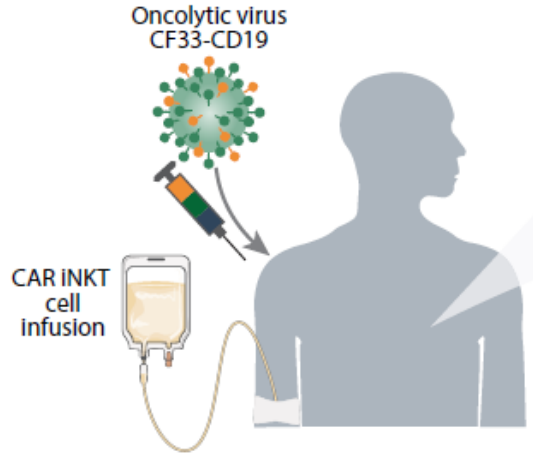
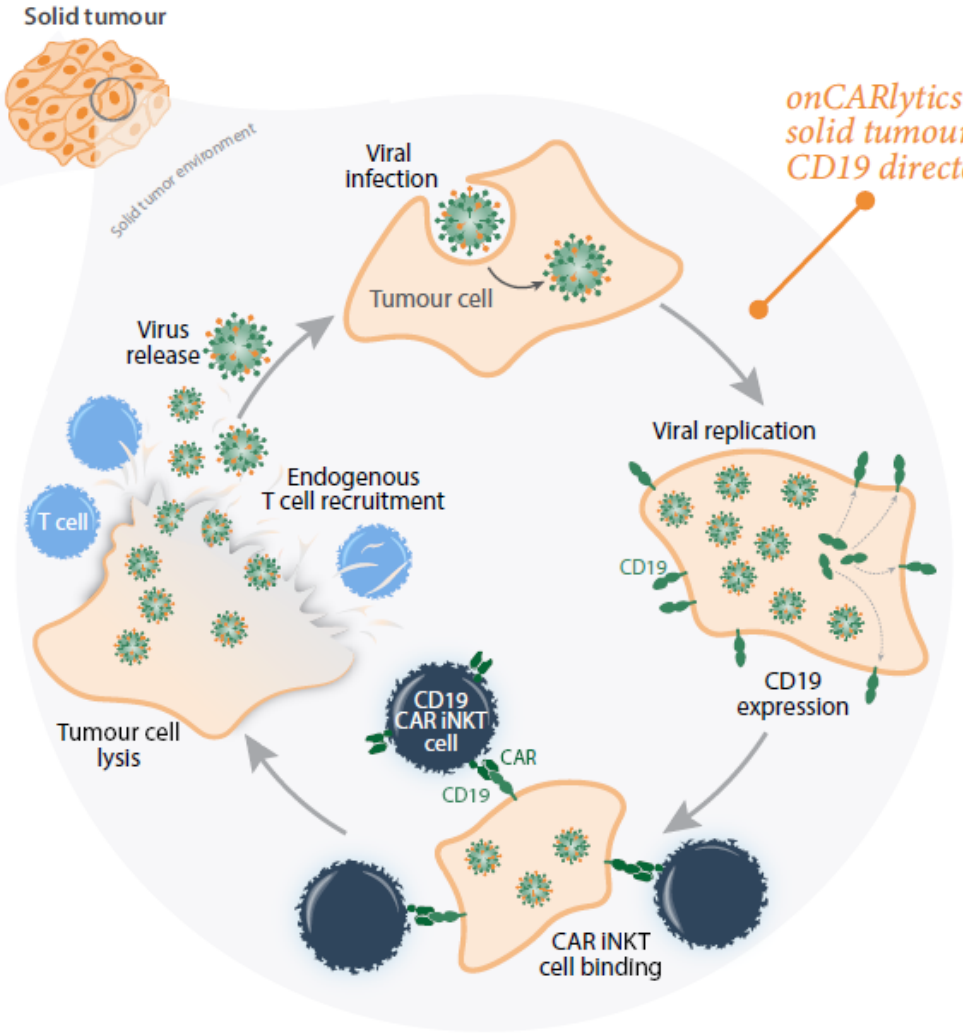
ALA-101 + onCARlytics Mechanism of Action



The research collaboration progressed to *in vivo* testing based on promising *in vitro* results



onCARlytics makes solid tumours "seen" by CD19 directed therapies

1. OnCARlytics infects tumour cells
2. Virus replication and production of CF33-CD19 on the cell surface enabling CD19 targeting
3. Tumour cell lysis leads to viral particle release and the combination promotes endogenous immune cell recruitment to tumours
4. Released viral particles re-initiate virus infection of surrounding tumour cells.

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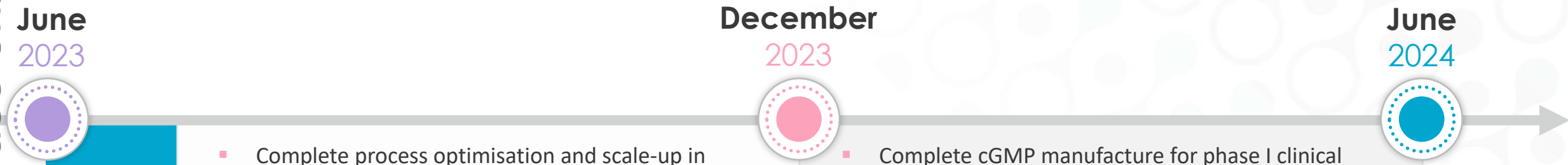
Milestones FY2024

- Arovella expects to advance ALA-101 into a phase I first-in-human clinical trial during 2024
- Arovella also continues to assess novel complimentary technologies to expand the use of the iNKT platform to treat solid tumours



	June 2023	December 2023
ALA-101	▪ Complete process optimisation and scale-up in preparation for cGMP manufacture ▪ Complete production of cGMP lentiviral vector ▪ Finalise clinical trial plan for phase I study	▪ Complete cGMP manufacture for phase I clinical trials ▪ Complete preparatory activities for phase I study, including submission of regulatory dossier.
iNKT Cell Therapy Platform	▪ Confirm the activity of CAR19-iNKT cells when combined with Imugene's onCARlytics to target solid tumours in animal model ▪ Analyse additional CARs to add to the platform ▪ In-licence cytokine technology currently under option (pending positive data)	▪ Initiate proof-of-concept testing for novel CARs and/or cytokine technology to expand iNKT platform for treatment of solid tumours

Arovella Has a Strong Leadership Team

LEADERSHIP

Dr. Michael Baker
CEO & MANAGING DIRECTOR

Dr. Nicole van der Weerden
CHIEF OPERATING OFFICER

Dr. Mini Bharathan
SENIOR VP DEVELOPMENT & TRANSLATIONAL MEDICINE

Dr. Robson Dossa
SENIOR DIRECTOR MANUFACTURING & QUALITY

Ana Radeljevic
BUSINESS DEVELOPMENT

BOARD OF DIRECTORS

Dr. Tom Duthy
BOARD CHAIR

Dr. Elizabeth Stoner
DIRECTOR

Dr. Debora Barton
DIRECTOR

Mr. Gary Phillips
DIRECTOR

Mr. David Simmonds
DIRECTOR

Summary – Arovella's CAR-iNKT Cell Platform

A 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 I clinical trials, expected to commence in 2024

CAR-iNKT cells have multiple anticancer properties
CAR-iNKT cells are dual-targeting with enhanced cancer killing ability

Arovella has an expanding pipeline
Arovella continues to enter collaborations and licence agreements to expand use of the iNKT platform to treat solid tumours

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

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Share Purchase Plan (SPP) Details

- Oversubscribed Placement raised $4.1 million (before costs)
- The SPP Offer price is the same as the Placement price at $0.045 per share
- The Offer price represents a 10% discount to the last closing share price prior to the announcement of the Placement on 2 June 2023
- The SPP is open from 15 June 2023, closing date is **29 June 2023**
- Minimum of $2,500 and up to $30,000 for current eligible shareholders
- There are no transaction or brokerage costs to participating shareholders
- The funds raised under the SPP will be used to:
  - progress Arovella's lead product, ALA-101, towards a phase 1 clinical trial for patients with CD19-positive haematological cancers;
  - strengthen Arovella's iNKT cell therapy pipeline;
  - pay for the costs of the SPP; and
  - general working capital purposes.

Thank You

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CEO & Managing Director

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