



arovella
T H E R A P E U T I C S

ASX: ALA

ANNUAL GENERAL MEETING

November 2022

Arovella Board of Directors



Dr. Liz Stoner
INTERIM CHAIRPERSON

Dr. Stoner is a distinguished biopharma executive, who brings decades of international industry experience to her role, including senior roles in Clinical Development Operations at Merck Research Laboratories. Liz is an Executive Partner at MPM Capital, and she has held numerous leadership roles at MPM portfolio companies. Liz was previously an Assistant Professor of Paediatrics at Cornell University Medical College..



Mr. David Simmonds
DIRECTOR

David was a senior audit partner with Ernst & Young from 1989 to 2017. From 2008 to 2013, David led the Capital Markets desk in Australia with responsibility for overseeing or reviewing all Australian cross border fundraisings. David was a member of the Board of MS Research Australia.



Dr. Michael Baker
CEO & MANAGING DIRECTOR

Over 15 years experience in scientific research, drug development and venture investing sectors. He was an Investment Manager with the leading Australian life science fund, BioScience Managers. He also conducted due diligence to shortlist investment opportunities and played an active role in managing portfolio companies.



Dr. Debora Barton
DIRECTOR

Dr. Barton has over 20 years of oncology experience, in academia, as a practicing physician and in the biotechnology / pharmaceutical industry. Served in key senior executive positions, including Carisma Therapeutics and TScan Therapeutics, where Dr. Barton is currently the Chief Medical Officer, and Advanced Accelerator Applications, acquired by Novartis during Debora's tenure

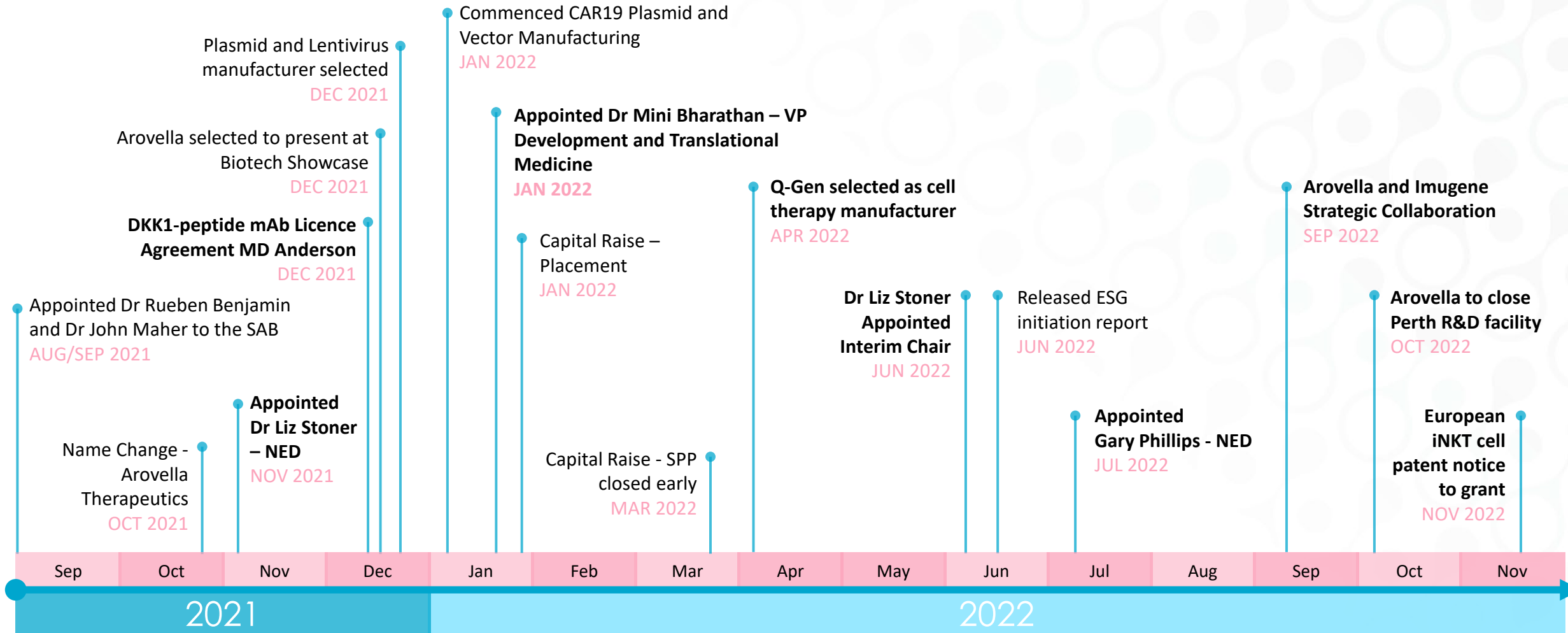


Mr. Gary Phillips
DIRECTOR

Mr. Phillips has more than 30 years of operational management experience in the pharmaceutical and healthcare industry in Europe, Asia and Australia. He is currently the CEO and Managing Director of the ASX-listed company, Pharmaxis — previously he was the CEO at Ciba Geigy in Hungary (Merged to form Novartis in 1996) where he led the successful launch of a portfolio of new products.



Recent Milestones



Arovella Company Overview

Financial Snapshot

ASX CODE	ALA
Market capitalisation ¹	\$16.7 million
Shares on issue	669.8 million
52-week low / high	\$0.020 / \$0.057
Cash (Sep 30 2022) ²	\$5.3 million

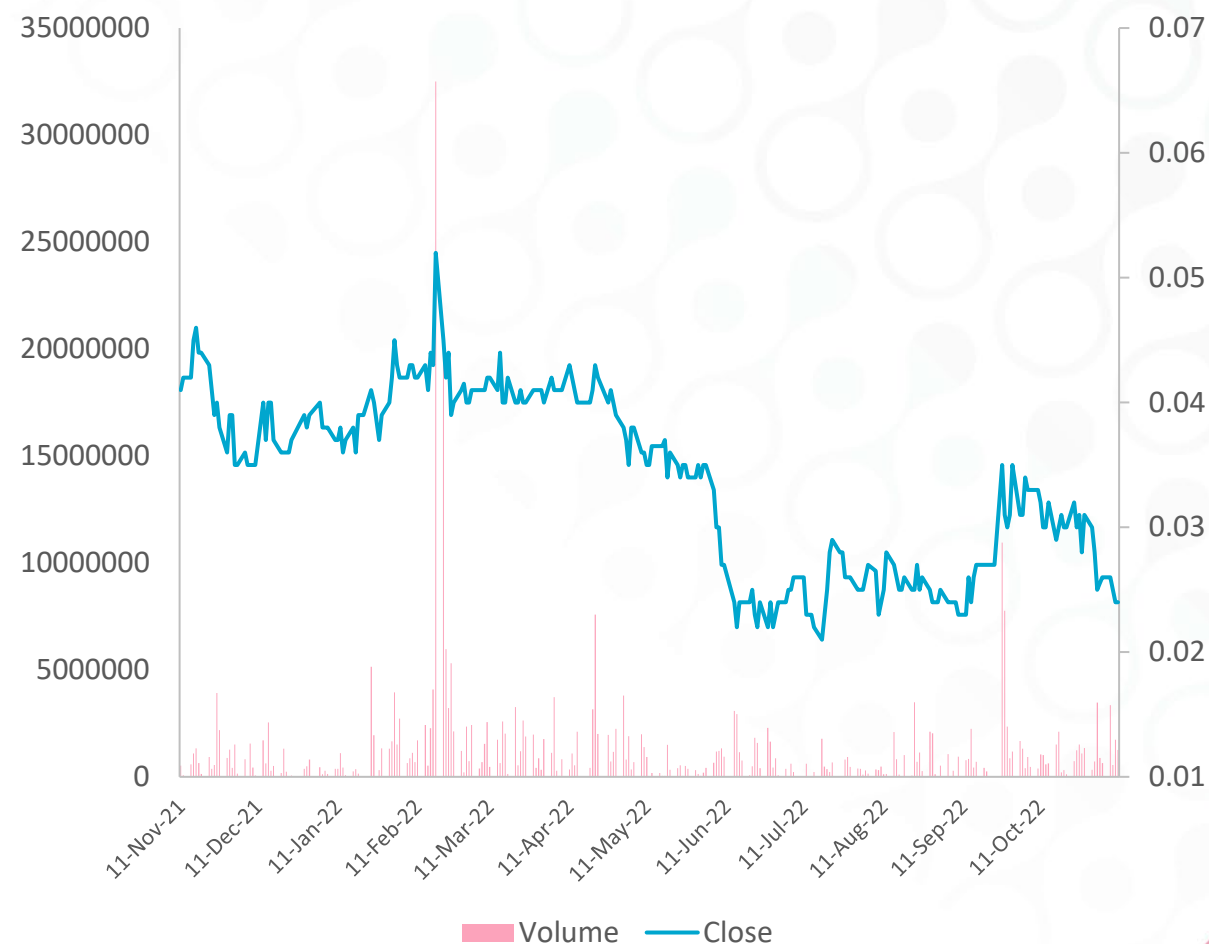
1. As of 11 Nov 2022

2. Including the FY 2022 R&D tax rebate expected to be ~\$1m

Major Shareholders

Shareholder	Ownership (%) ¹
THE TRUST COMPANY (AUSTRALIA) LTD	47,546,657 (7.18%)
MANN BEEF PTY LTD	20,000,000 (3.02%)
UBS NOMINEES PTY LTD	15,064,640 (2.28%)
DYLIDE PTY LTD	12,500,000 (1.89%)
KAMALA HOLDINGS PTY LTD	11,500,000 (1.74%)

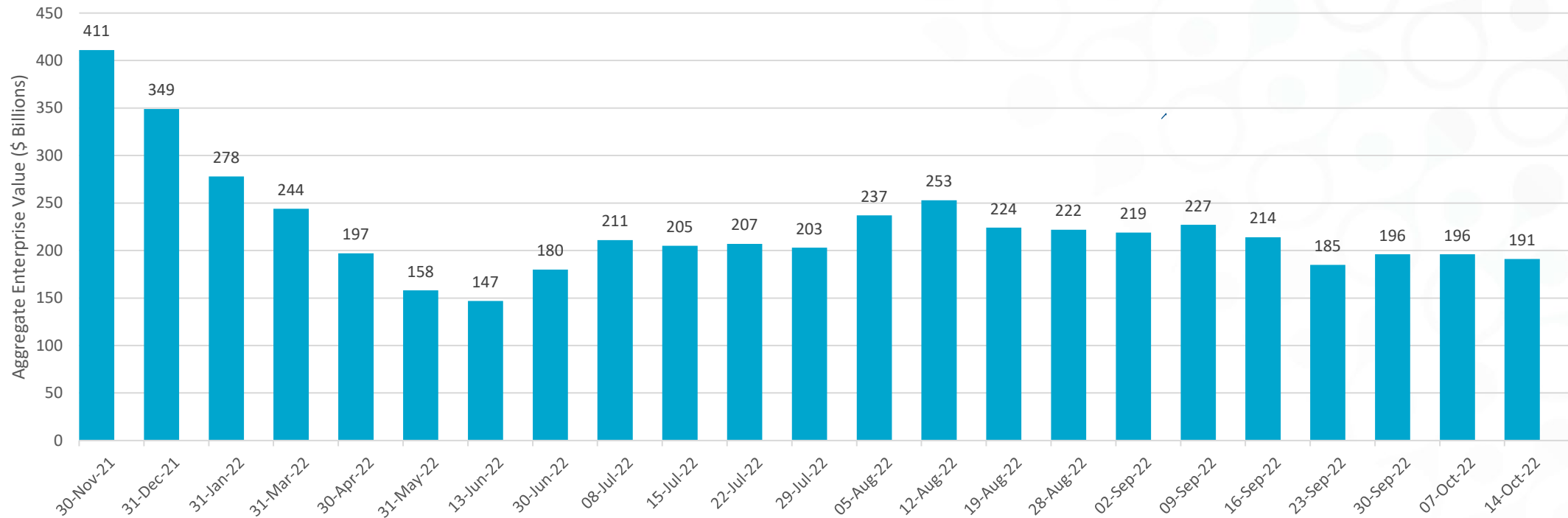
ALA Price and Volume - 12 Months¹



Biotech Sector Global Performance

- As of October 2022, global biotech enterprise values were down 68% since the 2021 peak and down 45% year to date¹
- In October 2022, 228 Life Science companies were trading at negative enterprise values ¹

Total Enterprise Value of Publicly Traded Global Biotech, 30 Nov, 2021 to 14 Oct, 2022 (\$ Billions)



1. Adapted from https://torreya.com/publications/Torreya_Biopharma_Market_Update_-_Oct_17__2022.pdf

Cancer Continues to be a Major Health Issue



Worldwide, an estimated 19.3 million new cancer cases (18.1 million excluding non-melanoma skin cancer) occurred in 2020¹



Cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020²



The global cancer therapeutics market is expected to reach \$366 billion by 2030, from \$167 billion in 2021, growing at a CAGR of 9.1%³

1. <https://pubmed.ncbi.nlm.nih.gov/33538338/>

2. <https://www.who.int/news-room/fact-sheets/detail/cancer>

3. <https://www.globenewswire.com/en/news-release/2022/04/04/2415940/0/en/Cancer-Therapeutics-Market-Size-to-Surpass-US-365-99-Bn-by-2030.html>

Cell Therapy Revolution to Treat Cancer

Recent Media Attention – Feb & May 2022

CNN health Life, But Better Fitness Food Sleep Mindfulness Relationships Edition ▾ 🔍 🌐 ☰

T-cell immunotherapy tied to 10-year remission in two leukemia patients, study finds

First patients of pioneering CAR T-cell therapy 'cured of cancer'

Cancer-killing cells still present 10 years on, with results suggesting therapy is a cure for certain blood cancers



Science journal Nature reveals decade-long remissions; sparks hope for curative potential of CAR-T treatment

Health & Biotech

February 11, 2022 | Special Report

ABC NEWS Melbourne Change location

Just In Watch Live Coronavirus Politics World Business Analysis Sport Science Health

SCIENCE

Leukaemia-fighting CAR T-cells kept patients in remission for 10 years — and counting

ABC Science / By science reporter Belinda Smith
Posted Thu 3 Feb 2022 at 5:30am

NEWS

First CAR T-cell child celebrates cancer cure

by: Peyton Kennedy
Posted: May 12, 2022 / 06:34 PM EDT
Updated: May 12, 2022 / 06:34 PM EDT

World's first recipient of Car-T cancer therapy is now 17
Emily Whitehead welcomes news Car-T is available to Irish children with leukaemia
© Fri, Apr 29, 2022, 02:00

A group photo of Emily Whitehead and her family, including her mother, father, and two sisters, standing outdoors in a park-like setting.

Published May 12, 2022

10 Years Cancer-Free! Emily Whitehead, Now 17, the First Child Cancer Patient to Receive Revolutionary CAR T-Cell Therapy, Celebrates Major Milestone



Emily Whitehead, First Pediatric Patient to Receive CAR T-Cell Therapy, Celebrates Cure 10 Years Later

Whitehead received life-saving treatment at CHOP, under the care of Dr. Stephan Grupp, transforming the field of cancer immunotherapy

11-May-2022 9:55 AM EDT, by Children's Hospital of Philadelphia [Contact Patient Services](#)

iNKT Cell Therapy Platform

**Imperial College
London**



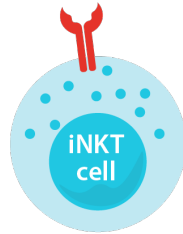
CAR-iNKT Cell Therapy Production and Advantages

Manufacturing

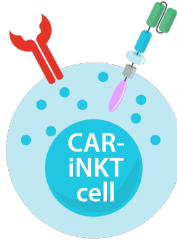
Collect Healthy Donor Blood



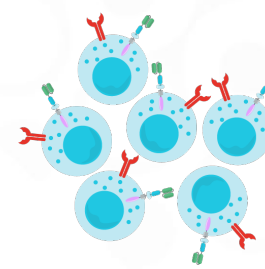
Isolate iNKT cells



Reprogram iNKT cells to produce a CAR



Expand CAR-iNKT cells to grow billions of cells



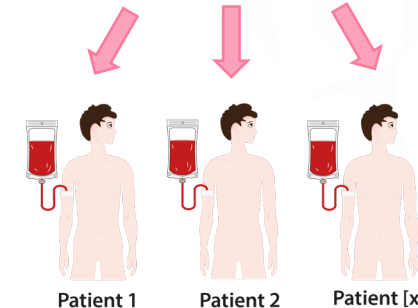
Vial and freeze CAR-iNKT cells



Thaw CAR-iNKT cells



Dose eligible patients



Dosing

Allogenic Manufacturing Advantages

1. Healthier Starting Material
2. Scalable Manufacturing with Reduced Costs – reach more patients
3. Faster Access for Aggressive Cancers
4. Removes Risk of Manufacturing Run Failure

CAR-iNKT Cells are Engineered to Enhance Activity


	APPROVED CAR-T CELLS	CAR-NK CELLS	CAR-iNKT CELLS
Subpopulation of T cells with NK cell properties	✗	✗	✓
Intrinsic anti-cancer receptor (dual targeting)	✗	✗	✓
Naturally suppress GVHD	✗	✗	✓
Allogeneic, 'off-the-shelf' dosing	✗	✓	✓
Low risk of CRS or neurotoxicity	✗	✓	✓
Minimal genetic engineering for off the shelf	✗	✓	✓
Persistence	✓	TBD	TBD ¹

CAR – Chimeric Antigen Receptor; iNKT – invariant Natural Killer T Cell; CRS – Cytokine Release Syndrome; TBD – To Be Determined

1. Spontaneous secondary remission observed in preclinical animal models

Arovella Therapeutics Pipeline

Cell Therapy

	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1		PHASE2/3 ¹		PARTNER
ALA-101 (CAR19-iNKT)	CD19 expressing cancers	CD19 Expressing Lymphoma						
ALA-101 + CF33-CD19	Solid tumours	Solid Tumours						 IMUGENE Developing Cancer Immunotherapies
ALA-104 (DKK1-CAR-iNKT)	Multiple Myeloma	Multiple Myeloma & Solid Tumours						

- Arovella is decommissioning its Perth OroMist research and development facility¹
- Following the site closure, all resources will be dedicated to Arovella's iNKT cell platform
- Arovella is reviewing its contractual arrangements relating to ZolpiMist and will continue to keep shareholders updated in this regard
- Arovella continues to screen for new technologies synergistic with the current platform or that have standalone potential

1. As announced 26 October, 2022

CAR19-iNKT (ALA-101)

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

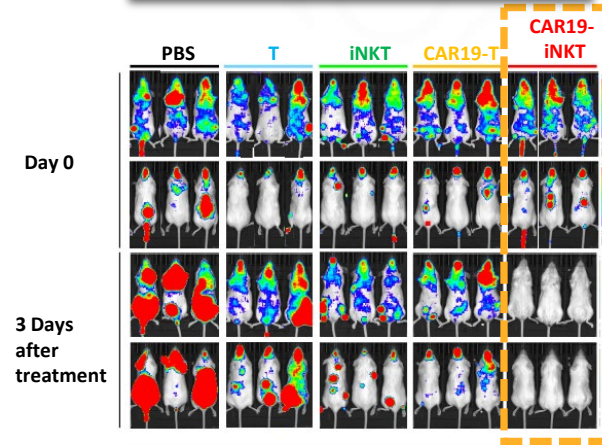


ALA-101: CAR19-iNKT Cells to Treat Blood Cancers

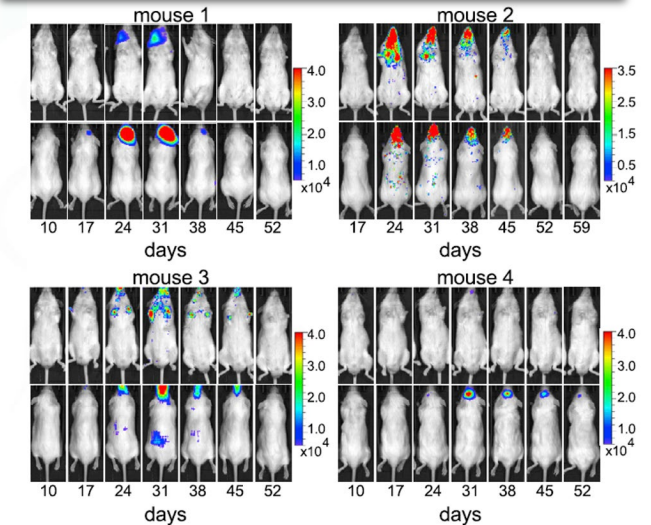
- ALA-101 is anticipated to be an effective, off-the-shelf cell therapy for the treatment of CD19 expressing cancers
- Our data validates the use of iNKT cells as a treatment for CD19 expressing cancer types
- ALA-101 is more efficient at clearing tumour cells than conventional cell therapies when the cancers produce CD1d and CD19
- Our therapy results in better animal survival than conventional cell therapies
- ALA-101 results in a spontaneous secondary remission and the data suggests iNKT cells can cross the blood brain barrier

CAR19-iNKT Outperforms Conventional Therapies

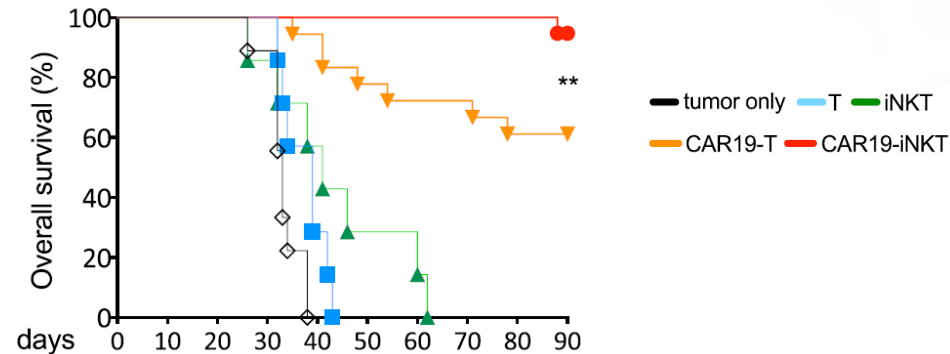
Faster Killing of Cancer Cells That Have CD1d



Spontaneous Secondary Remission



Increased Survival Over CAR-T Cells



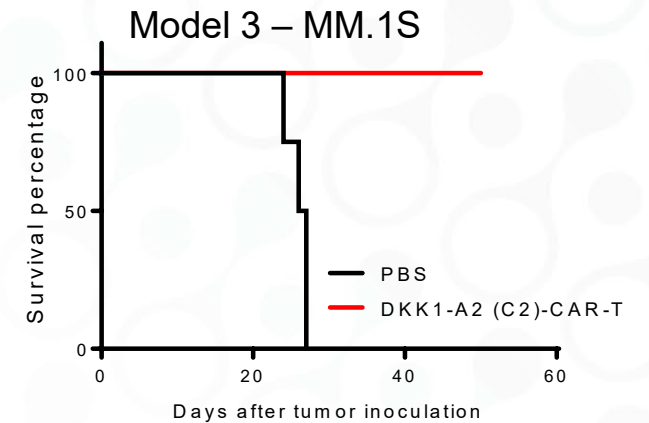
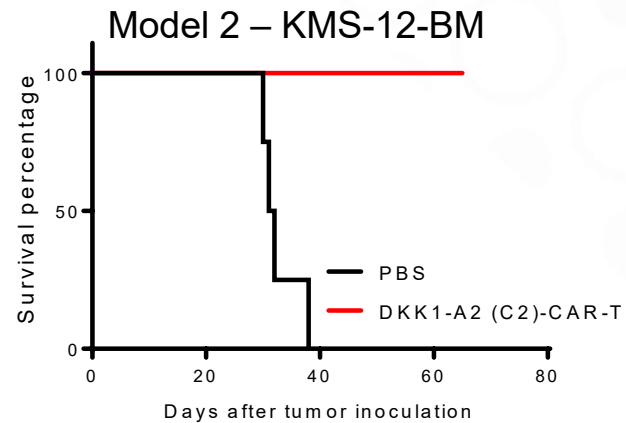
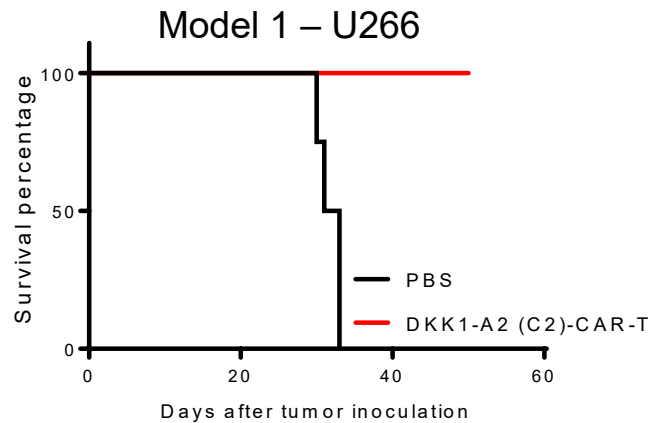
DKK1-CAR-iNKT (ALA-104)

An off-the-shelf cell therapy for multiple myeloma (blood cancer)
and potentially solid tumours



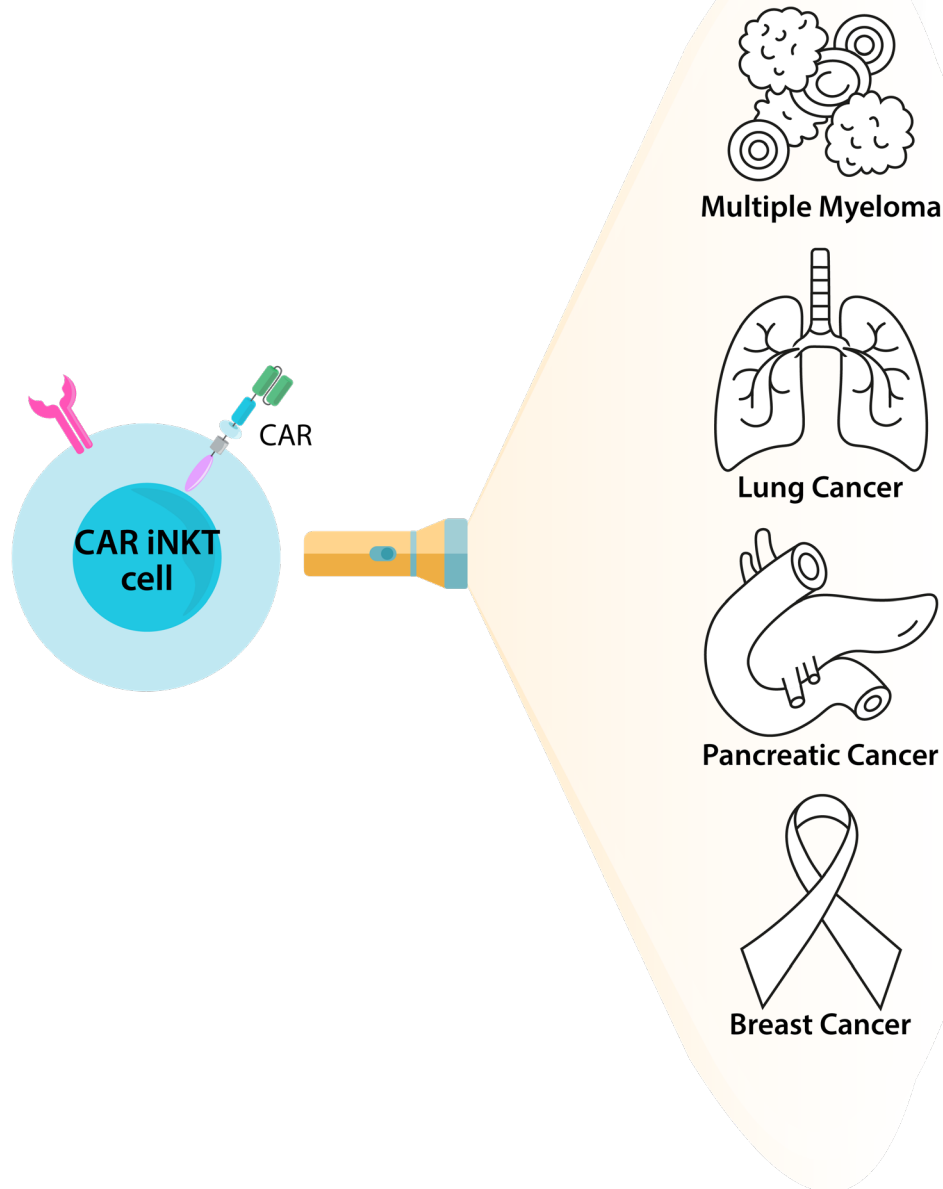
DKK1-CAR-T Cell Activity in Multiple Myeloma

DKK1-CAR-T cells were tested in three different animal models for multiple myeloma, displaying robust activity in all standard models



- » All treated mice were alive at 50-60 days, while untreated mice succumbed to the cancer at 30-40 days
- » Multiple myeloma cells also express CD1d, so including DKK1-CAR into iNKT cells will make them dual targeting
- » DKK1-CAR-T cells also have activity in animal models for **lung, pancreatic and triple negative breast cancer**

Potential Application of ALA-104



- DKK1-CAR-T cells display robust activity in animal models against multiple myeloma, lung cancer, pancreatic cancer and triple negative breast cancer
- Once we generate DKK1-CAR-iNKT cells, we will test them against blood cancers and solid tumours



IMUGENE

Developing Cancer Immunotherapies



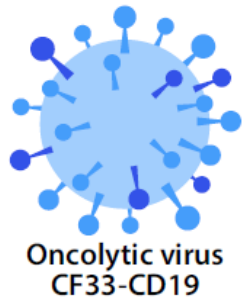
CF33-CD19 + CAR19-iNKT

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



Combining CAR19-iNKT and CF33-CD19 (onCARlytics)

- CF33 is an oncolytic virus that targets tumour cells and not healthy cells
- The virus was developed at City of Hope by Professor Yuman Fong
- Dr Saul Priceman has engineered CF33 to induce CD19 production after tumour cells have been infected
- Phase 1 trials for CF33 commenced October 2021 with CHECKvacc and May 2022 with VAXINIA

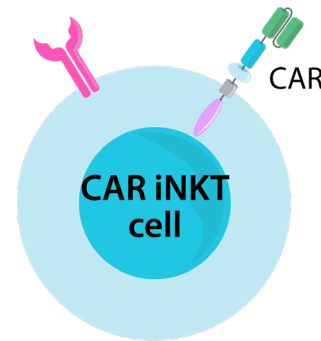


IMUGENE
Developing Cancer Immunotherapies



City of
Hope®

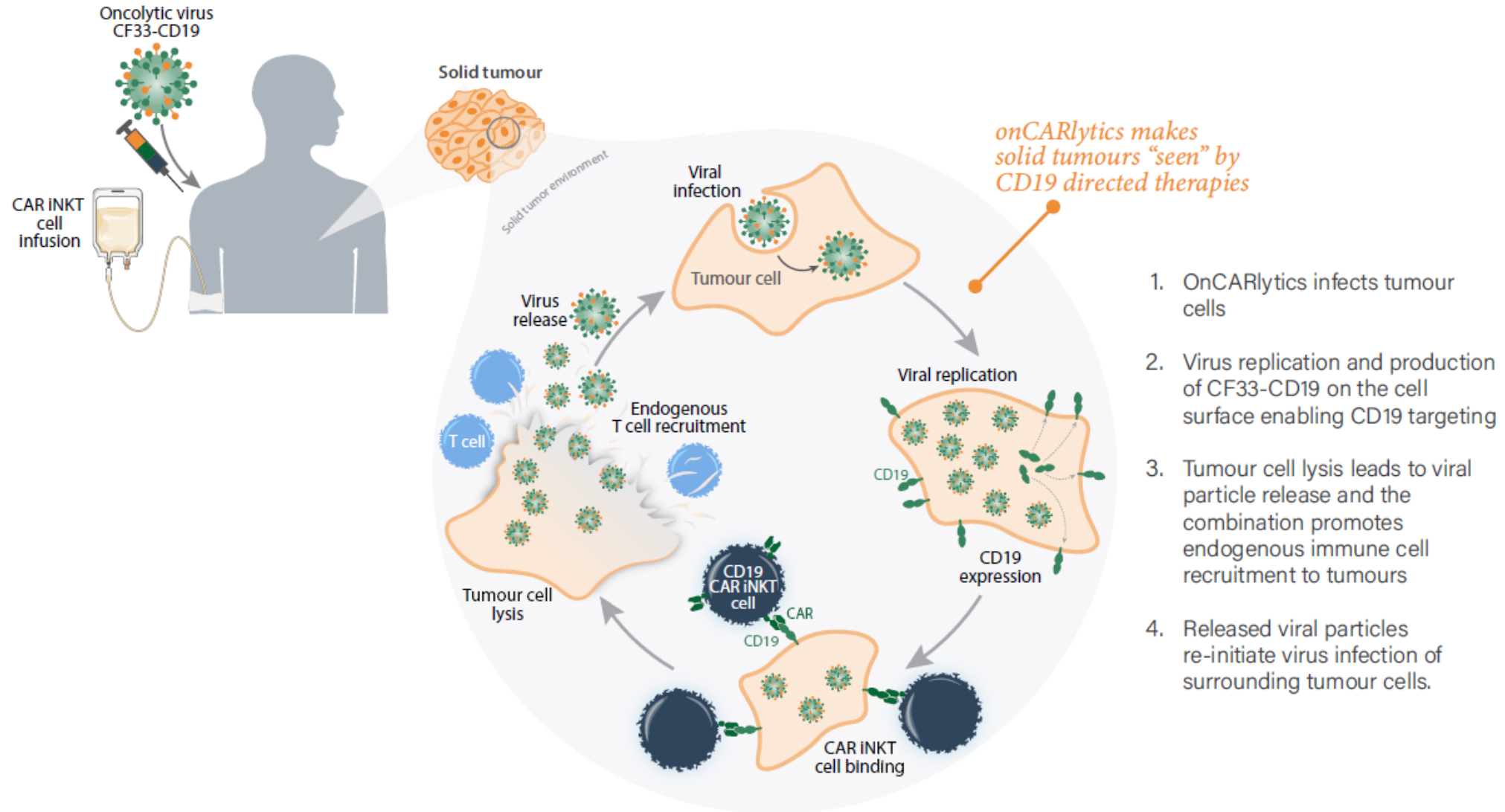
- CAR19-iNKT cells are very potent and are rapidly activated to kill CD19 expressing cancer cells
- The product is being developed as an off-the-shelf product for cancer treatment
- The platform was developed by Professor Tassos Karadimitris at Imperial College London



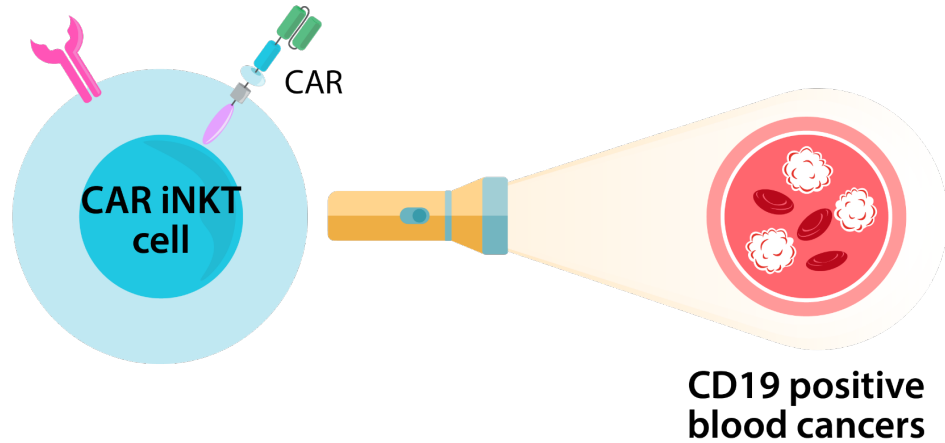
arovella
T H E R A P E U T I C S

**Imperial College
London**

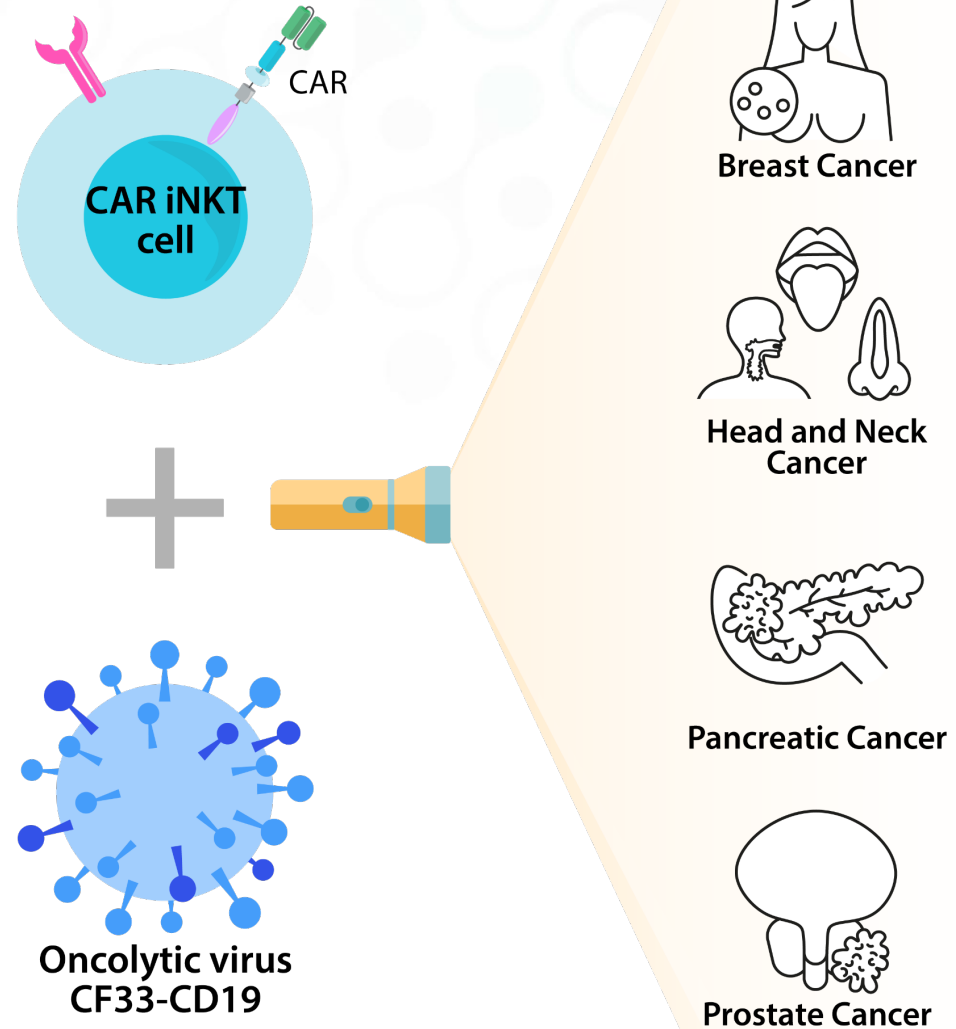
What is the Mechanism of Action?



Expanding ALA-101's Utility



- We expect CAR19-iNKT cells to be effective against blood cancers that naturally produce CD19
- Combining CF33-CD19 with CAR19-iNKT cells opens up the possibility of treating a range of solid tumours



Upcoming Milestones FY23

Activity for Arovella (now to June 2023)	Therapy	Complete (CY)
▪ Strategic planning outcomes	Company Wide	Completed
▪ Complete process development and confirmation manufacturing runs for CAR19-iNKT	ALA-101	Q2 2023
▪ Finalise CAR19-iNKT and onCARlytics Agreement and study setup	ALA-101/CF33-CD19	Q4 2022
▪ Complete <i>in vitro</i> (test tube) study to assess CAR19-iNKT cell activity against CD19 producing solid cancer cells	ALA-101/CF33-CD19	Q1 2023
▪ Complete <i>in vivo</i> (mouse) studies to assess CAR19-iNKT cell activity against solid tumours in an animal model	ALA-101/CF33-CD19	Q2 2023
▪ Complete target validation studies for DKK1-CAR-iNKT	ALA-104	Q1 2023
▪ Complete <i>in vitro</i> (test tube) and <i>in vivo</i> studies (mouse) for DKK1-CAR-iNKT against multiple myeloma and solid tumours	ALA-104	Q2 2023
▪ Optimise CAR Candidate to complete IND enabling studies	ALA-104	Q2 2023
▪ Search for potential world class therapeutic assets focused on cancer treatment	Company Wide	Ongoing

Company Wide

ALA-101

ALA-101 + CF33-CD19

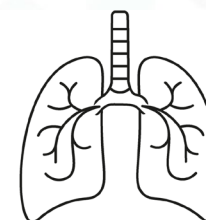
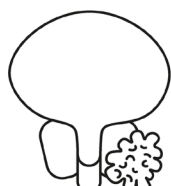
ALA-104

Arovella's Potential Cancer Targets

ALA-101

ALA-101 + CF33-CD19

ALA-104



Non-Hodgkin's Lymphoma ¹	Head and Neck Cancer ²	Prostate Cancer ³	Brain Metastases ^{4,5}	Triple Negative Breast Cancer ⁶	Pancreatic Cancer ⁷	Lung Cancer ⁸	Multiple Myeloma ⁹
80,470 cases in the US per annum	66,470 cases in the US per annum	268,490 cases in the US per annum	150-200,000 cases in the US per annum	28,150 cases in the US per annum	62,210 cases in the US per annum	236,740 cases in the US per annum	34,470 cases in the US per annum
73.8% 5-year survival rate	58-75% 5-year survival rate	96.8% 5-year survival rate	3-47 month survival	76.9% 5-year survival rate	11.5% 5-year survival rate	22.9% 5-year survival rate	57.9% 5-year survival rate

1. <https://seer.cancer.gov/statfacts/html/nhl.html>

2. <https://www.cancer.net/cancer-types/head-and-neck-cancer/statistics>

3. <https://seer.cancer.gov/statfacts/html/prost.html>

4. <https://www.mdanderson.org/cancer-types/brain-metastases.html>

5. <https://ascopubs.org/doi/10.1200/JCO.20.01255>

6. <https://www.cancer.org/cancer/breast-cancer/about/types-of-breast-cancer/triple-negative.html>

7. <https://seer.cancer.gov/statfacts/html/pancreas.html>

8. <https://seer.cancer.gov/statfacts/html/lungb.html>

9. <https://seer.cancer.gov/statfacts/html/mulmy.html>

Arovella Therapeutics Summary



World Leading Partners

Arovella licenced its iNKT Cell Therapy Platform from **Imperial College London** and its DKK1 mAb/CAR from **MD Anderson** and is collaborating with **Imugene**



Data Driven

Arovella uses data to drive decision making for its key assets and clinical indications



Allogeneic Platform, Two Targets

Arovella is developing off the shelf cell therapies for CD19 expressing lymphomas and solid tumours, and DKK1 producing cancers.



World Class Team

Arovella continues to build a team with deep experience in drug development, particularly cell therapies



Acquiring New Technologies

Arovella continues to focus on sourcing, evaluating and acquiring innovative technologies that align with key focus areas



Growth Potential

Arovella is the only ASX listed company working with an iNKT cell therapy platform and the only company worldwide with CAR technology targeting a DKK1 peptide

Thank You

Dr. Michael Baker

CEO & Managing Director

Email: mbaker@arovella.com

Mobile: +61 403 468 187





Committed to helping people live longer and healthier lives

Patient-Centric

It starts with the end in mind. In our case, it is our patients. At Arovella, we are invested in making a positive difference in helping patients live longer and healthier lives. Creating a brighter future for people is our driving force.

Data-driven and Milestone Focused

Behind all life-changing therapies is excellent, ground-breaking science. We utilise data to shape our decisions to enable us to reach our set milestones

Accountable, Honest and We Act With Integrity

Our mission of helping patients focuses us. We hold ourselves to account for our actions. We strive to do what is right for all of our stakeholders.

We Are Persistent and Never Give Up

Drug development is a challenging arena. We are committed to our mission of helping patients, and we will continue to push each other through positive and challenging times in the pursuit of developing life-changing therapeutics.

Disclaimer

1. The information in this presentation does not constitute personal investment advice. The presentation is not intended to be comprehensive or provide all information required by investors to make an informed decision on any investment in Arovella Therapeutics Limited (**Company**). In preparing this presentation, the Company did not take into account the investment objectives, financial situation and particular needs of any particular investor.
2. Further advice should be obtained from a professional investment adviser before taking any action on any information dealt with in the presentation. Those acting upon any information without advice do so entirely at their own risk.
3. Whilst this presentation is based on information from sources which are considered reliable, no representation or warranty, express or implied, is made or given by or on behalf of the Company, any of its directors, or any other person about the accuracy, completeness or fairness of the information or opinions contained in this presentation. No responsibility or liability is accepted by any of them for that information or those opinions or for any errors, omissions, misstatements (negligent or otherwise) or for any communication written or otherwise, contained or referred to in this presentation.
4. Neither the Company nor any of its directors, officers, employees, advisers, associated persons or subsidiaries are liable for any direct, indirect or consequential loss or damage suffered by any person as a result of relying upon any statement in this presentation or any document supplied with this presentation, or by any future communications in connection with those documents and all of those losses and damages are expressly disclaimed.
5. Any opinions expressed reflect the Company's position at the date of this presentation and are subject to change.
6. This document does not constitute an offer to sell, or a solicitation of an offer to buy, securities in the United States or any other jurisdiction in which it would be unlawful. In particular, the New Shares and Options have not been, and will not be, registered under the US Securities Act of 1933 (the "US Securities Act") and may not be offered or sold in the United States except in transactions exempt from, or not subject to, the registration requirements of the US Securities Act and applicable US state securities laws. The distribution of this presentation in jurisdictions outside Australia may be restricted by law and any such restrictions should be observed.
7. The New Shares and Options will be offered and sold in the United States only to (i) institutional accredited investors (as defined in Rule 501(a)(1), (2), (3) and (7) under the US Securities Act); and (ii) dealers or other professional fiduciaries organized or incorporated in the United States that are acting for a discretionary or similar account (other than an estate or trust) held for the benefit or account of persons that are not US persons and for which they exercise investment discretion, within the meaning of Rule 902(k)(2)(i) of Regulation S under the US Securities Act.