

ASX: ALA

Arovella Therapeutics Limited
ACN 090 987 250



ASX Release

24 February 2023

SPARK PLUS BIOTECH DAY PRESENTATION

Highlights

- **Arovella presents at Spark Plus Biotech Day in Singapore**

MELBOURNE, AUSTRALIA 24 February 2023: Arovella Therapeutics Ltd (ASX: ALA), is pleased to announce that its CEO And MD, Dr Michael Baker, will today present at the Biotech Day symposium in Singapore hosted by Spark Plus.

Dr Baker will present key pre-clinical data for Arovella's iNKT cell therapy platform and describe 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/investor-presentations>.

Release authorised by the Managing Director and Chief Executive Officer of Arovella Therapeutics Limited.

Dr Michael Baker

Chief Executive Officer & Managing Director

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NOTES TO EDITORS:

About Arovella Therapeutics Ltd

Arovella Therapeutics Ltd (ASX: ALA) is a biotechnology company focused on developing therapies to treat human diseases. Arovella is 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. The Company is also commercialising ZolpiMist™, a first-in-class oral spray of zolpidem tartrate to treat short-term insomnia. ZolpiMist is approved by the FDA and the TGA and is marketed in the USA. Arovella has rights to the product outside of the US and Canada.

For more information, visit www.arovella.com.



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

ASX:ALA

BIOTECH DAY

February 2023

Spark+

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Arovella Therapeutics Highlights



Off-the-Shelf iNKT Cell Platform

Arovella is developing off-the-shelf iNKT cell therapies for CD19 expressing lymphomas and solid tumors, and DKK1 producing cancers



Data Driven

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



World Leading Partners

Arovella's technologies are licensed from **Imperial College London** and **MD Anderson Cancer Center**. Arovella has an ongoing collaboration with **Imugene**



Strategic Acquisitions

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



Strong Leadership Group

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



Unique Value Proposition

Arovella is among few companies globally developing an iNKT cell therapy platform, and the only company developing a CAR targeting a DKK1-peptide

Cell Therapy Has Revolutionized Blood Cancer Treatment

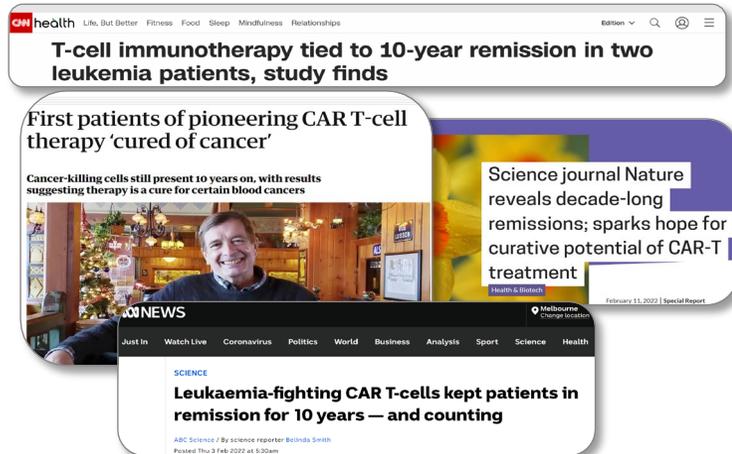
- CAR-T cells have demonstrated ability to **cure** haematological cancers

BUT.....

- Manufacturing, logistics and access have prevented broader patient uptake and relapse rates have been documented to occur in 40-60% of patients¹

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

February 2022



May 2022



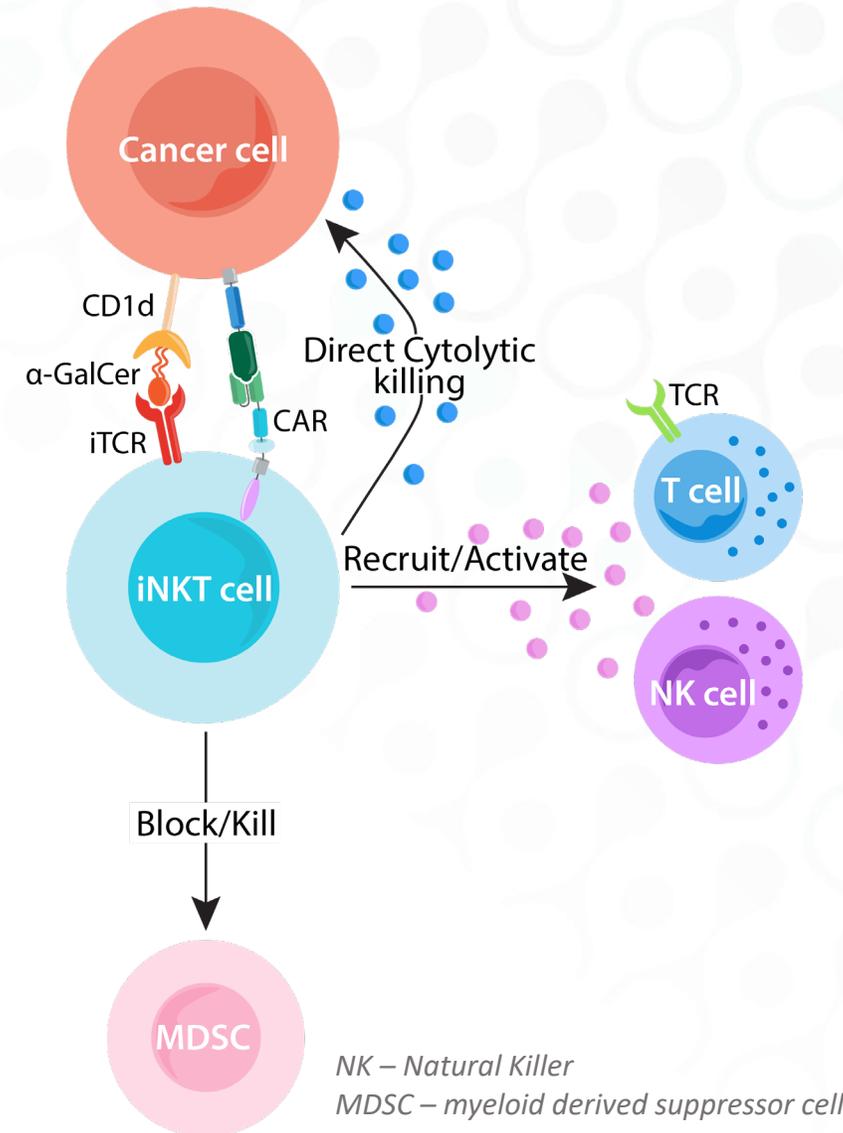
Product	Approval Year	2022 Revenue
	2017	US\$1160m ²
	2017	US\$536m ³

1. Larson RC, Maus MV, 2021. Recent advances and discoveries in the mechanisms and functions of CAR T cells. *Nat Rev Cancer*, **21**(3): 145-161. 10.1038/s41568-020-00323-z
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

iNKT Cells are Primed to Kill Cancer

- invariant Natural Killer T (iNKT) cells have evolved to target and kill certain cancer cells¹
- The invariant T Cell Receptor (TCR) does not change between people and iNKT cells are protective against graft versus host disease (GvHD)^{2,3}
- The cells can be administered “off-the-shelf”
- Shape the tumor microenvironment, promoting tumor destruction⁴
- Recruit other components of the immune system to attack cancer cells⁵
- The addition of a Chimeric Antigen Receptor (CAR) makes them dual targeting, enhancing cytotoxicity⁶
- CAR-iNKT cells mount a rapid response and display robust tumor killing *in vivo*⁶

1. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5743650/>
2. <https://pubmed.ncbi.nlm.nih.gov/28824628/>
3. <https://ashpublications.org/blood/article/127/14/1828/34747/Larger-number-of-invariant-natural-killer-T-cells>
4. <https://www.frontiersin.org/articles/10.3389/fimmu.2022.999549/full>
5. <https://link.springer.com/article/10.1007/s00441-010-1023-3>
6. <https://pubmed.ncbi.nlm.nih.gov/30300581/>



NK – Natural Killer
MDSC – myeloid derived suppressor cell

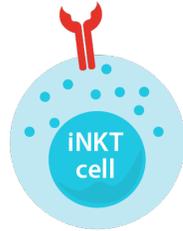
CAR-iNKT Cell Therapy Production Advantages

Manufacturing

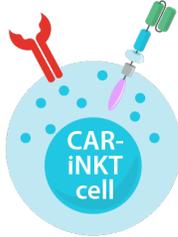
Collect Healthy Donor Blood



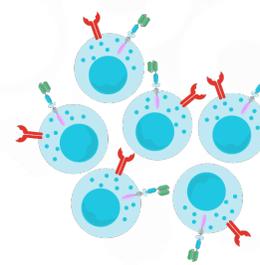
Isolate iNKT cells



Reprogram iNKT cells to produce a CAR



Expand to grow billions of CAR-iNKT cells



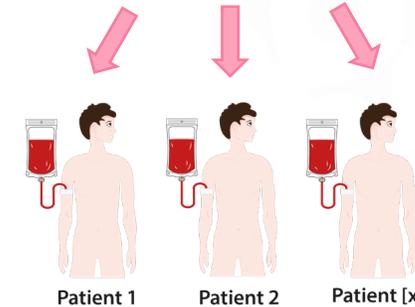
Vial and freeze CAR-iNKT cells



Thaw CAR-iNKT cells



Dose eligible patients

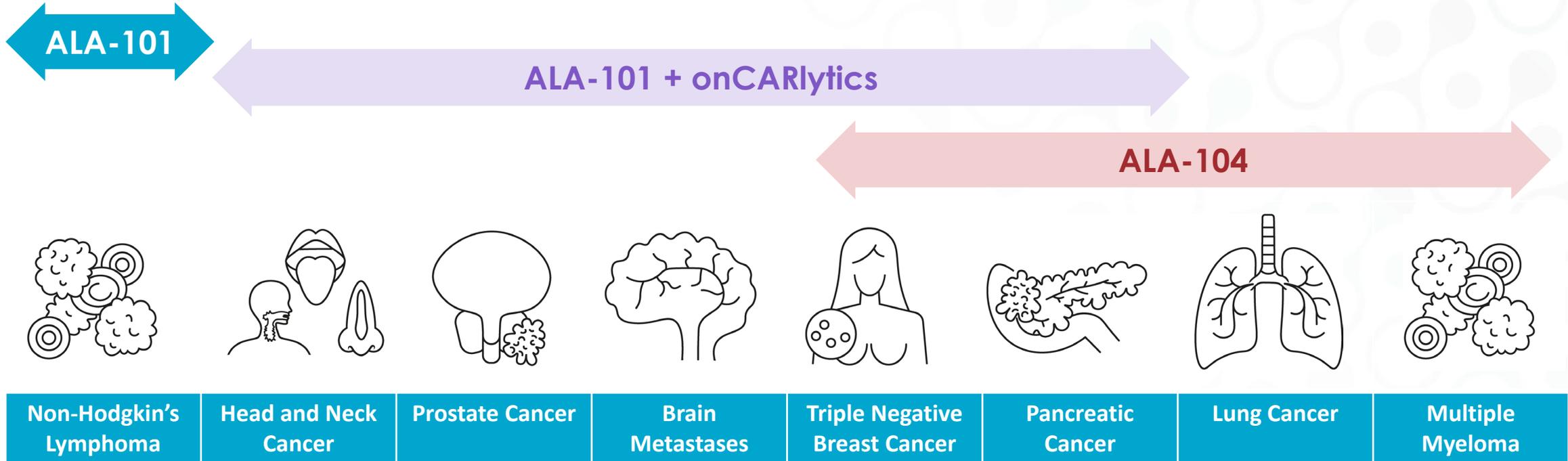


Treatment

Allogeneic Manufacturing Advantages

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

Arovella's Potential Cancer Targets



Arovella Therapeutics Cell Therapy Pipeline

Cell Therapy							
	Partner	Discovery	Lead Optimisation	IND-Enabling	Phase 1		
CAR19-iNKT (ALA-101)		CD19 Expressing Lymphoma					
ALA-101 + onCARlytics	 IMUGENE <small>Developing Cancer Immunotherapies</small>	Solid Tumors					
DKK1-CAR-iNKT (ALA-104)		Multiple Myeloma					
		TNBC					
		NSCLC					
		Pancreatic					

TNBC – triple negative breast cancer; NSCLC – non-small cell lung carcinoma

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

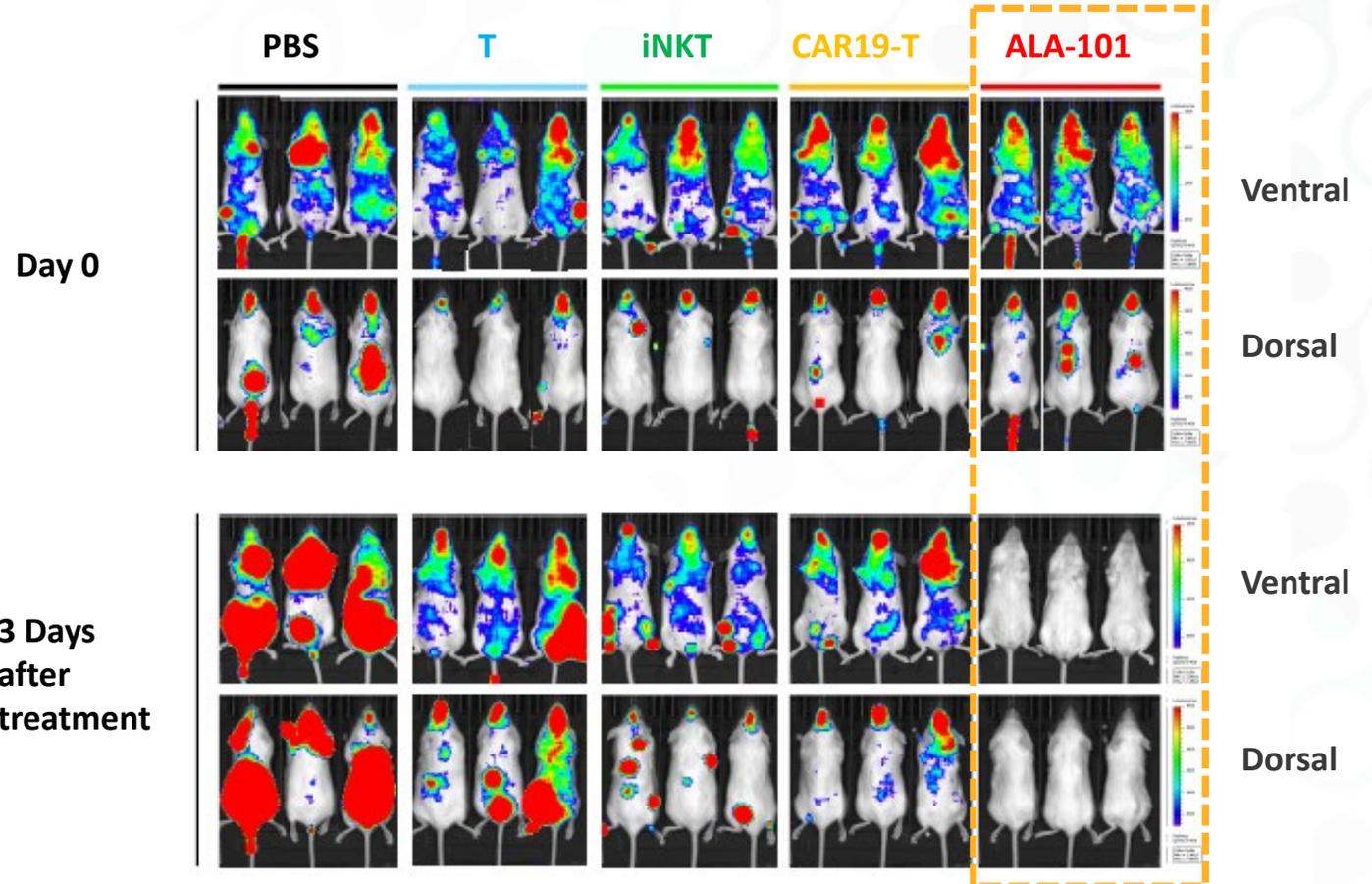
An off-the-shelf cell therapy for CD19 expressing cancers



ALA-101: Enhanced Tumor Killing *In Vivo*

ALA-101 rapidly eradicates tumor cells in mice

- Tumor 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 three days, ALA-101 resulted in significant regression of tumor cells
- In all other treatments, we observed strong tumor cell persistence
- ALA-101 displays swift action

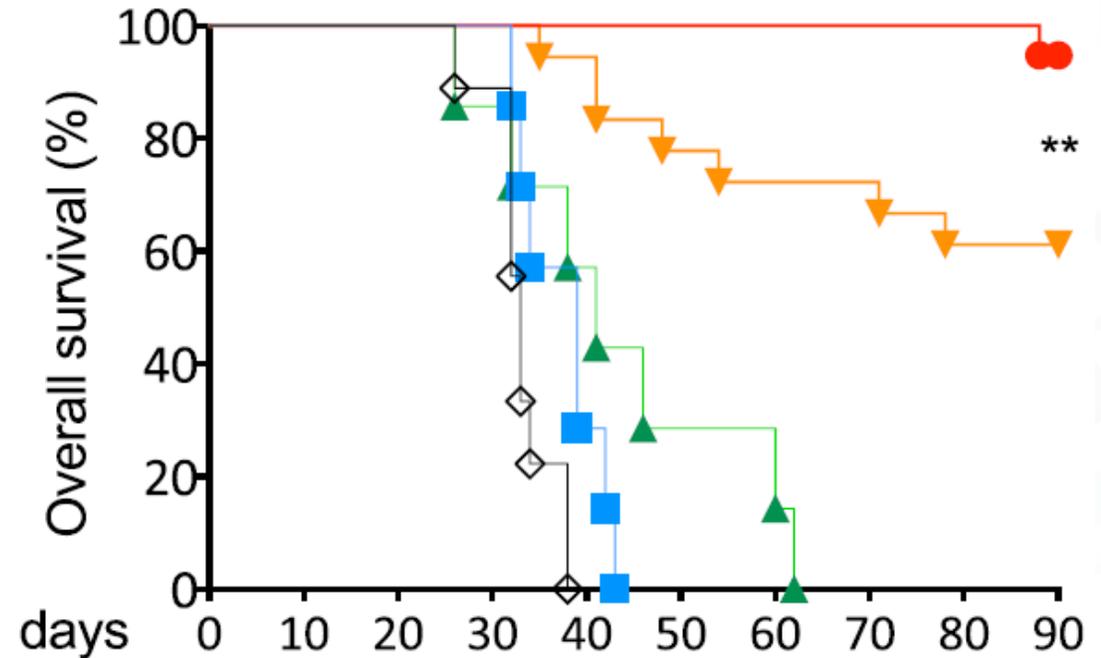


Rotolo *et al.*, Cancer Cell (2018)

ALA-101: Superior Animal Survival Over CAR-T Cells

ALA-101 significantly increased survival in mice versus treatment with CAR19-T cells

- Tumor 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**



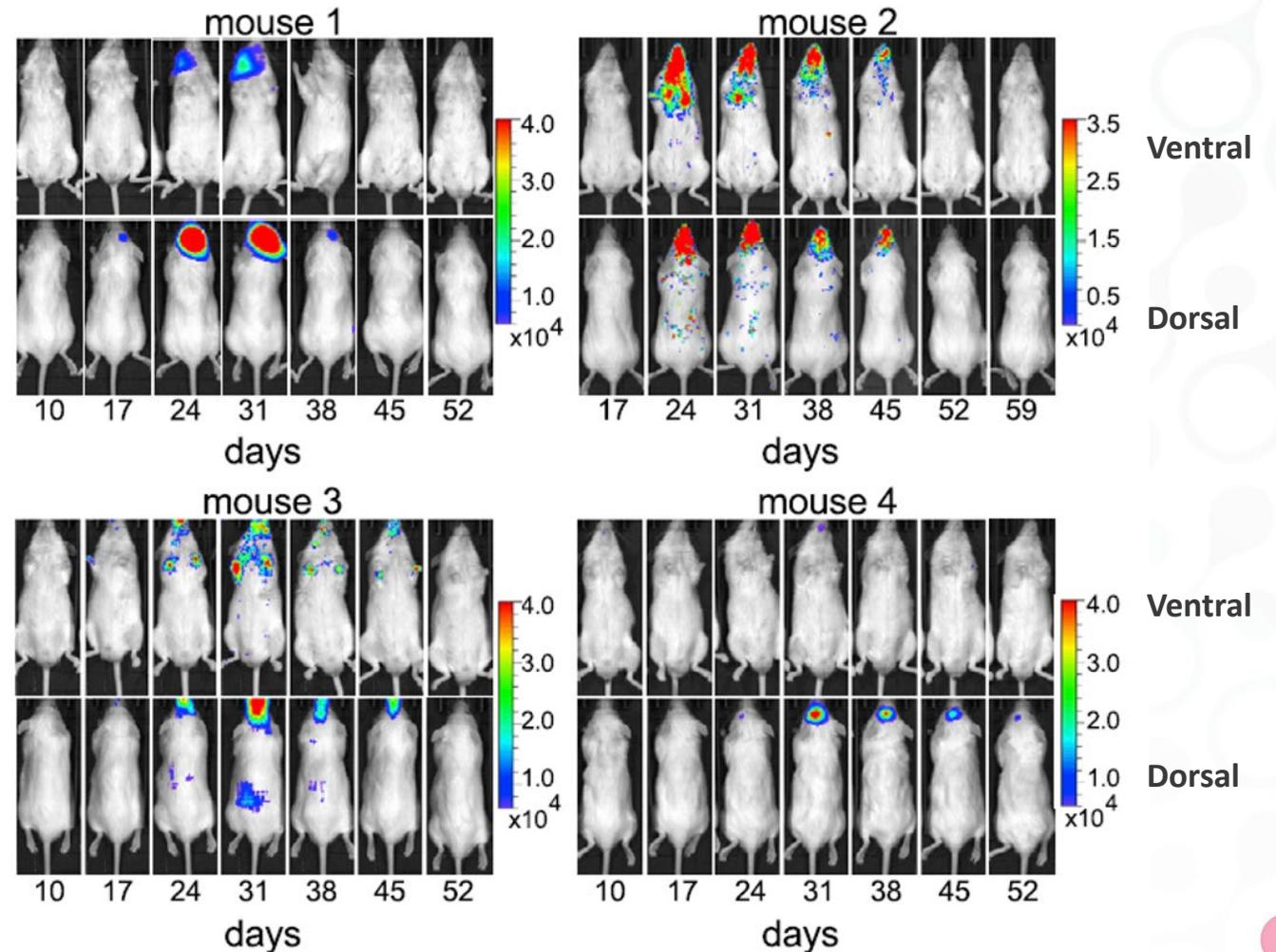
- PBS (saline) (n=12)
- T-cell (n=7)
- iNKT-cell (n=7)
- CAR19-T cell (n=19)
- ALA-101 (n=19)

Rotolo et al., Cancer Cell (2018)

ALA-101: Spontaneous Secondary Remission

ALA-101 activity may persist to eradicate tumor 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 infers 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)



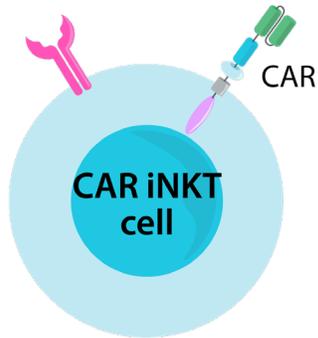
ALA-101 + CF33-CD19

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



Combining ALA-101 and CF33-CD19 (onCARlytics)

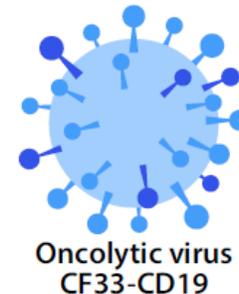
- ALA-101 is very potent and is rapidly activated to kill CD19 expressing cancers¹
- The product is being developed as an off-the-shelf product for cancer treatment



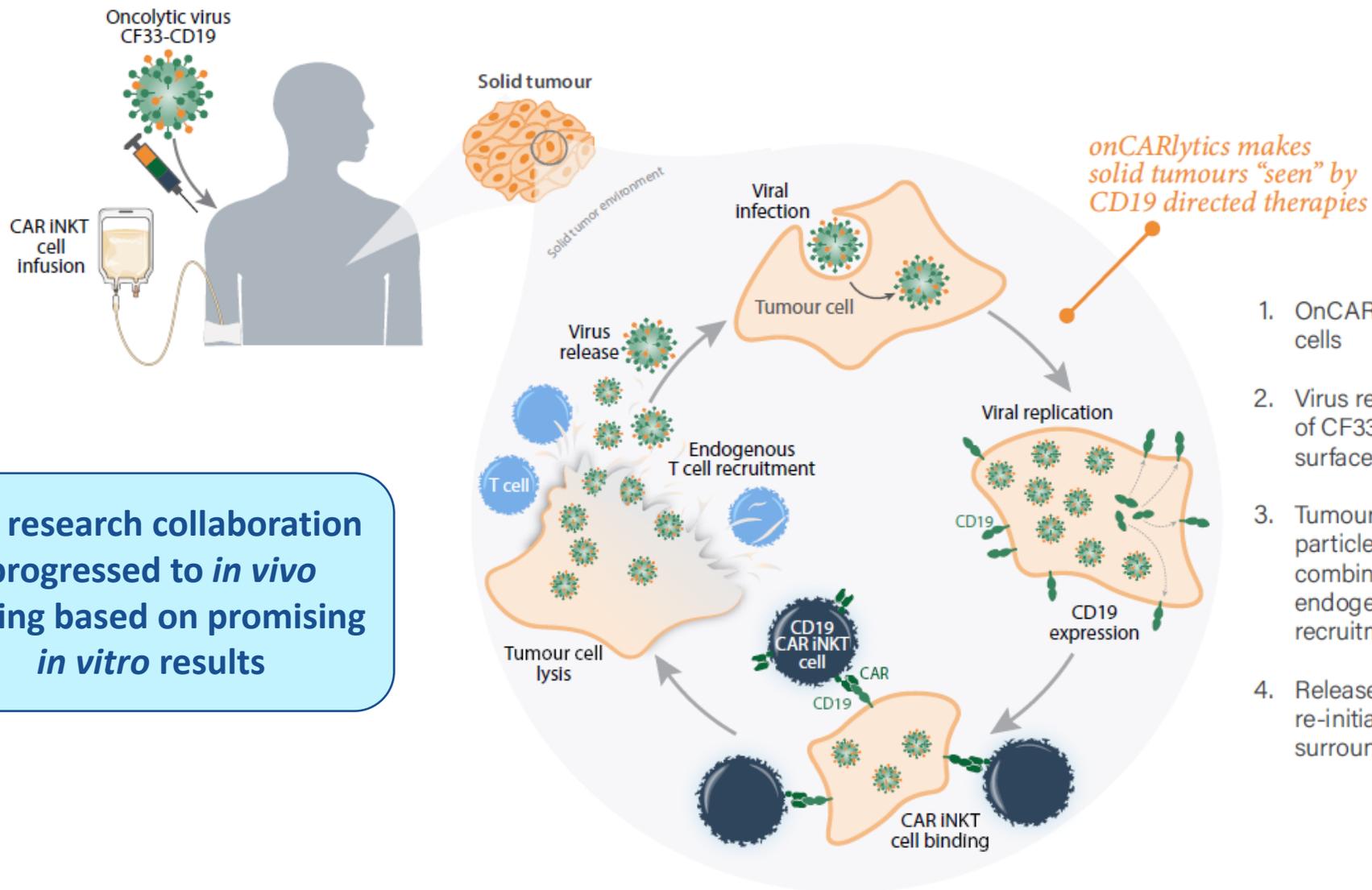
1. <https://pubmed.ncbi.nlm.nih.gov/30300581/>
2. <https://pubmed.ncbi.nlm.nih.gov/32032721/>
3. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9126033/>



- CF33 is an oncolytic virus that targets tumor cells²
- CF33 has been engineered to induce CD19 expression after tumor cells have been infected – onCARlytics³
- Phase 1 trials for CF33 commenced October 2021 with CHECKvacc and May 2022 with VAXINIA



ALA-101 + onCARlytics Mechanism of Action



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

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. Sandhya Buchanan
MANUFACTURING & QUALITY



Ana Radeljevic
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Imperial College London

Dr John Maher
CSO Leucid Bio

Dr Reuben Benjamin
Kings College London

Professor Qing Yi
Houston Methodist

Arovella's Key Milestones Over 18 Months

Cell Therapy					
	Partner	Discovery	Lead Optimisation	IND-Enabling	Phase 1
CAR19-iNKT (ALA-101)		CD19 Expressing Lymphoma			
ALA-101 + onCARlytics	 IMUGENE <small>Developing Cancer Immunotherapies</small>	Solid Tumors			
DKK1-CAR-iNKT (ALA-104)		Multiple Myeloma			
		TNBC			
		NSCLC			
		Pancreatic			

TNBC – triple negative breast cancer; NSCLC – non-small cell lung carcinoma

- Over the next 6-18 months Arovella plans to:
 - Complete clinical manufacturing of ALA-101
 - Commence Phase 1 clinical trial with ALA-101 for Non-Hodgkin's Lymphoma
 - Complete proof of concept studies and commence IND-enabling studies for ALA-101 + onCARlytics
 - Complete CAR-optimisation for IND enabling studies for ALA-104
 - Complete studies to assess the novel cytokine technology with the iNKT cell platform

Thank You

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