ASX Release

11 December 2023

CAR-iNKT CELL PLATFORM DATA PRESENTED AT ASH

- **New data utilising a different CAR-iNKT product, manufactured using Arovella's platform, supports the extended use of the CAR-iNKT cell platform against multiple tumour types**
- **Superior animal survival data from Arovella's CAR-iNKT Platform with CD28 co-stimulatory domain**
- **Data presented at the 65th American Society of Hematology (ASH) annual meeting in San Diego, California**

MELBOURNE, AUSTRALIA 11 December 2023: Arovella Therapeutics Ltd (ASX: ALA), a biotechnology company focused on developing its invariant Natural Killer T (iNKT) cell therapy platform, is pleased to announce its research collaborators from Imperial College London presented data using Arovella's CAR-iNKT cell therapy platform. Team members from Professor Karadimitris' lab have presented new data using the CAR-iNKT cell platform in a poster presented at the 65th Annual American Society for Hematology (ASH) conference in San Diego, California. The data released utilises Arovella's proprietary CAR-iNKT platform, which Professor Karadimitris pioneered.

The poster, presented by Dr Kanagaraju Ponnusamy, describes the use of the platform to produce CAR-iNKT cells targeting B-cell maturation antigen (BCMA) to eliminate Multiple Myeloma and describes the optimisation of the CAR construct. The work identified that the CD28 co-stimulatory domain (shown by the green line in the Kaplan Meier Survival Curve) was more effective than other co-stimulatory domains and led to substantially improved anti-tumour activity in mice. This CD28 co-stimulatory domain is also incorporated into Arovella's ALA-101 product.

Arovella's CEO and MD, Dr Michael Baker, spoke with Professor Karadimitris about the data. The presentation is attached to this release, and the interview is available on the Company's website https://www.arovella.com/investor-presentations and can be viewed here. The full poster is also available on the Company's website https://www.arovella.com/conference-presentations.

The data highlights the potential of the iNKT cell platform and demonstrates its broad applicability across multiple tumour types by incorporating different CARs. In addition, the data reflects the benefit of the CD28 co-stimulatory domain and its superiority over other co-stimulatory domains when used individually or in combination.

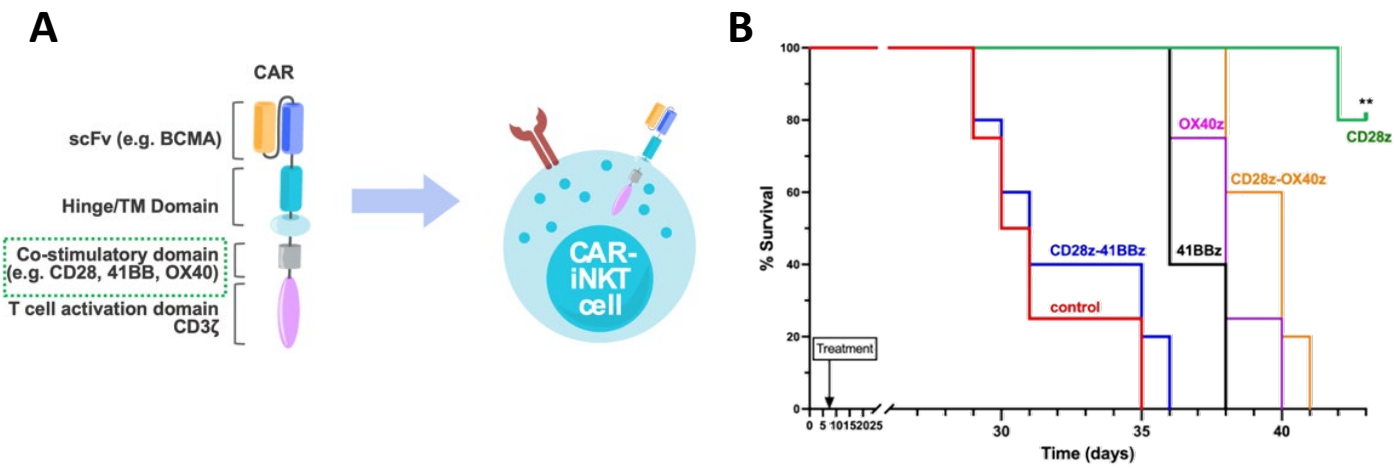

Figure 1. (A) A typical CAR structure consists of an scFv, Hinge/TM domain, co-stimulatory domain (focus of the study) and a T cell activation domain. **(B)** A Kaplan- Meier survival curve of NSG mice injected with $7x10^6$ MM1.S-luciferase cells and treated seven days later with $1x10^6$ iNKT cells transduced with an anti-BCMA CAR containing one of five different co-stimulatory domains as indicated. Disease burden was monitored by bioluminescence (** $p<0.01$; unpaired t-test).

Arovella's CEO and MD, Dr Michael Baker, commented, "It is excellent to see the additional data using the CAR-iNKT cell platform. We firmly believe in the platform's potential, and this data highlights there are avenues to expand the use of the platform in multiple tumour types. To have this accepted and presented at ASH is a testament to the exciting research that continues at Imperial College London and the promise of the iNKT cell platform."

For and on behalf of the Board and for further information, please contact:

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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 into solid tumour treatment through its CLDN18.2-targeting technology licensed from Sparx Group. Additional tumour targeting technologies are anticipated to be used in conjunction with Arovella's 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.

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

Arovella's proprietary CAR-iNKT manufacturing process

Arovella's process has distinct advantages for the production of CAR-iNKT cells

Imperial College London

Invented by Prof. Tassos Karadimitris

Licenced from Imperial College London in 2021

Patent protected until 2038

Granted in Europe and pending in USA, Canda, China, Hong Kong and Australia

High Transduction Efficiency

High proportion of cells express the chimeric antigen receptor (CAR), increasing potency

Transduction performed on low cell numbers, minimising requirement for expensive reagents

Maintains highly cytotoxic cell population

Method provides for rapid expansion of cells to produce multiple doses per batch and maintains specific phenotype associated with better tumor cell killing

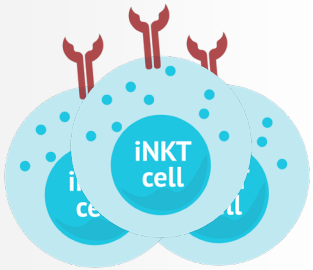
CAR-iNKT cell therapy production overview & advantages

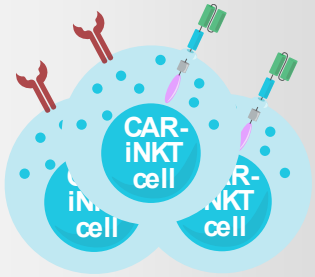
Off-the-shelf manufacturing advantages

MANUFACTURING

Collect Healthy Donor Blood

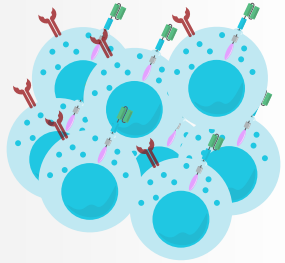
Isolate iNKT cells





Engineer iNKT cells to produce a CAR

Expand to grow billions of CAR-iNKT cells

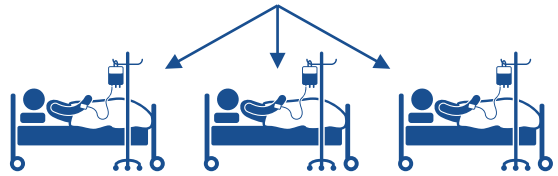


Vial and freeze CAR-iNKT cells

TREATMENT

Thaw CAR-iNKT cells

Dose eligible patients



Healthier starting material
Potentially better efficacy

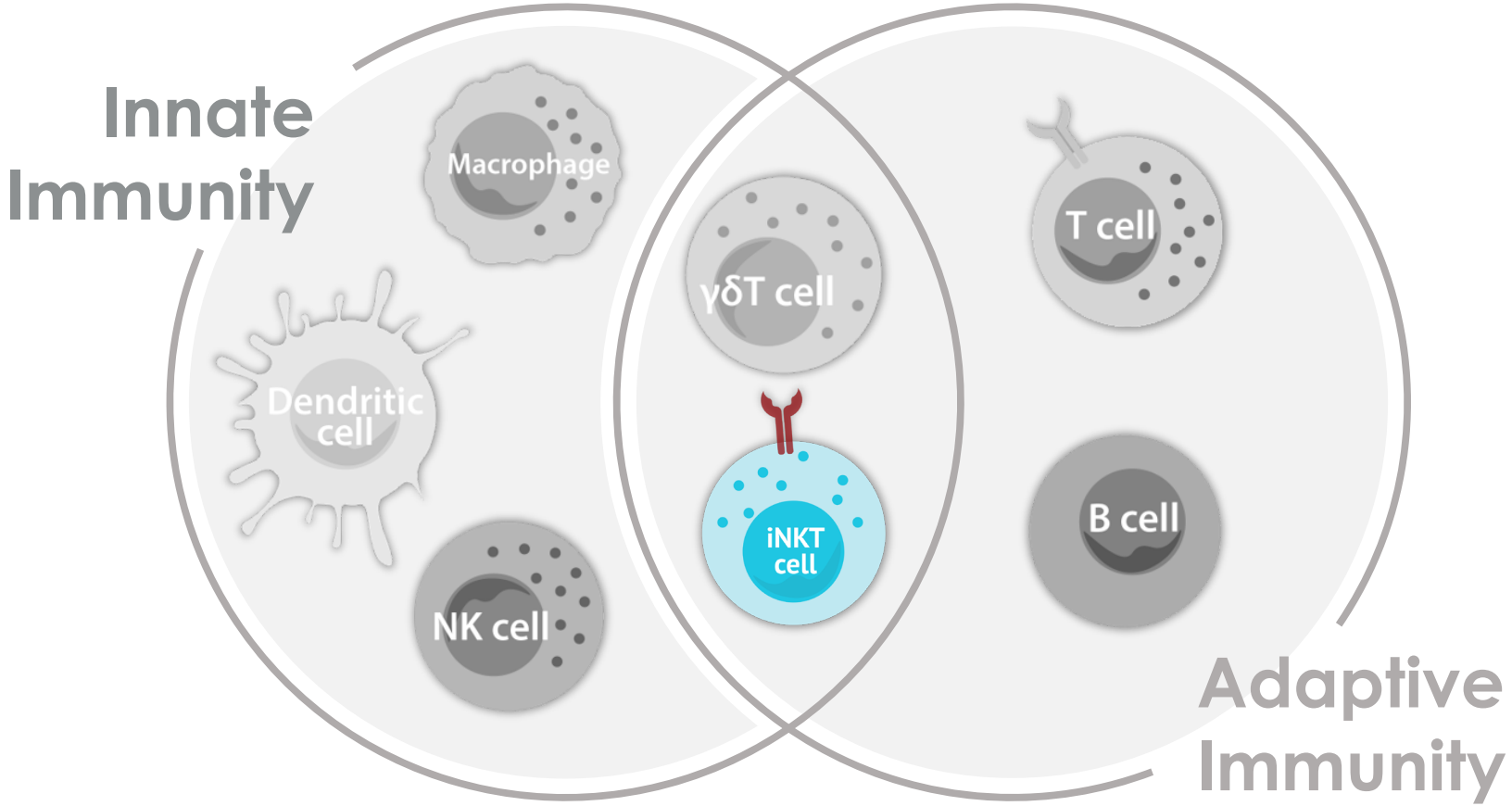
Scalable manufacturing with reduced costs
Reach more patients

Faster access to treatment
Improved outcomes for aggressive cancers

Removes risk of manufacturing run failure

iNKT cells represent a next-generation cell therapy

Properties make them ideal for use in cell therapy



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

Strong safety profile

- Don’t cause graft versus host disease (GvHD)

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

Cell therapies targeting blood cancers

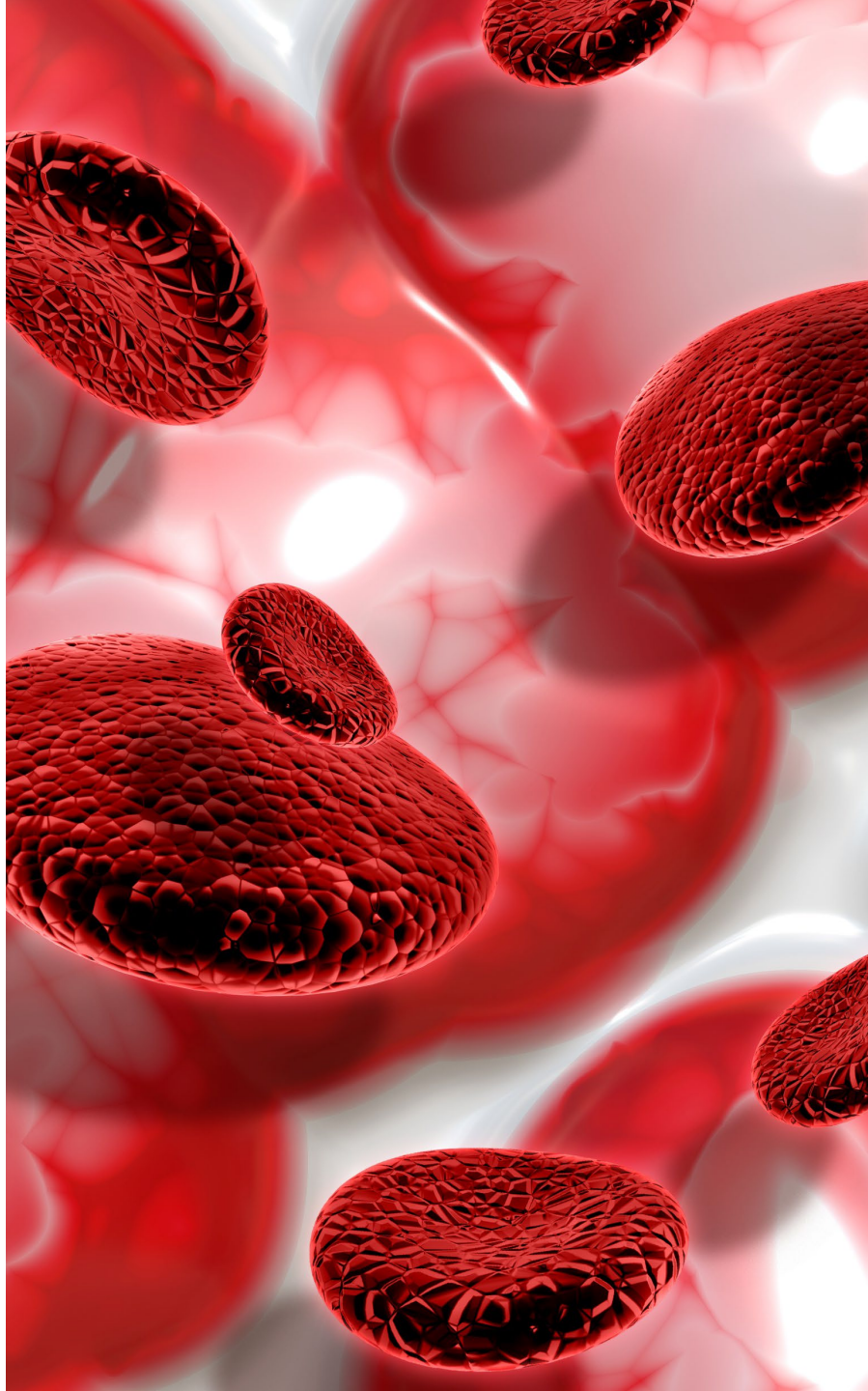
Approved CAR-T therapies target lymphoma/leukemia and multiple myeloma

CD19+ lymphomas and CD19+ leukemias

4 approved products available for use in the US	**>$2b in combined revenue** expected in 2023
CAR-T products are moving to second line therapy	**No allogeneic cell therapy** approved for CD19+ blood cancers

Multiple myeloma (MM; BCMA+)

2 approved products Available for use in the US	**>$800m in combined revenue** expected in 2023
First cell therapy approved in the US in 2021	**No allogeneic cell therapy** approved for MM



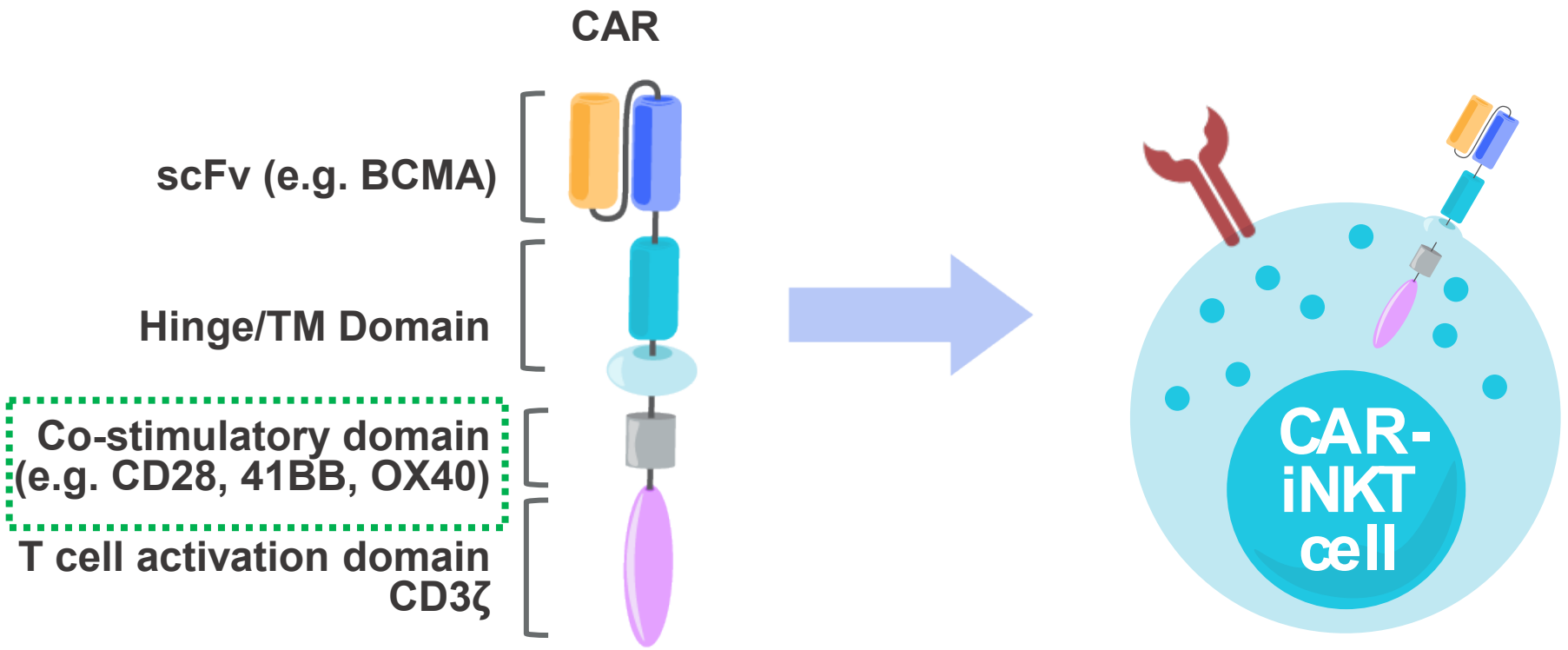
Prof. Tassos Karadimitris

Imperial College London

CAR-iNKT cells can target multiple myeloma

The co-stimulatory domain can be modified to drive increased activity

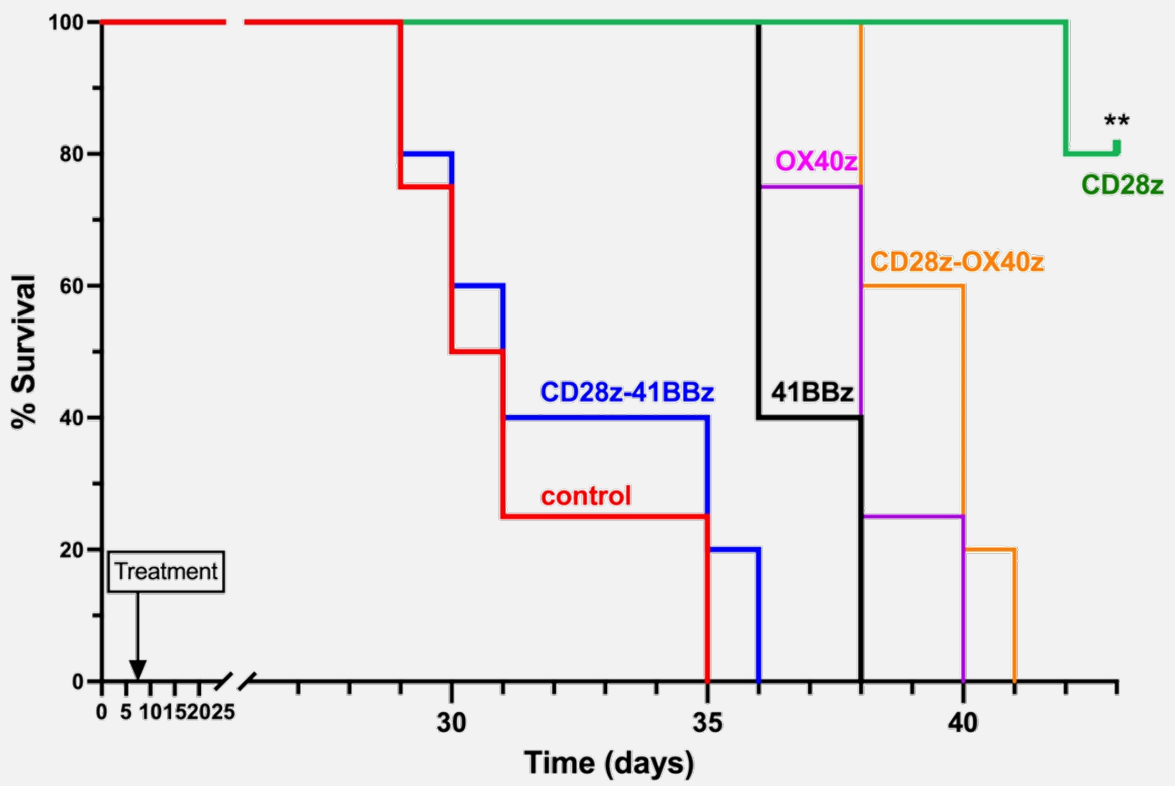
- Five BCMA-targeting CARs with different co-stimulatory domains were created for testing in a mouse model of multiple myeloma



CAR-iNKT cells can target multiple myeloma

Optimising the co-stimulatory domain of the BCMA CAR substantially improved efficacy

- MM1.S multiple myeloma tumour cells expressing BCMA were intravenously delivered into mice
- Mice were treated BCMA-iNKT cells including co-stimulatory domains:
  - No CAR
  - CD28z-41BBz
  - 41BBz
  - OX40z
  - CD28z-OX40z
  - CD28z
- After >41 days, only the mice treated with a CAR containing a CD28z co-stimulatory domain remained alive
- CD28z alone outperformed all other co-stimulatory domain combinations



ASH Poster 3459

Summary

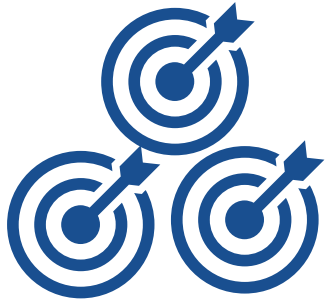
ASH presentation supports the breadth of Arovella's CAR-iNKT cell platform

Imperial College London

Arovella's iNKT cell platform has a unique and robust manufacturing pathway

Data shows that BCMA-CAR-iNKT cells can kill multiple myeloma tumour cells

Supports that Arovella's platform can be utilized to target multiple tumour types



Using the CD28z co-stimulatory domain

enables BCMA-CAR-iNKT cells to have better activity in comparison to other co-stimulatory domains

Both BCMA targeting CAR-T products contain a 4-1BB co-stimulatory domain

Arovella's iNKT cell therapy platform

is an exciting off-the-shelf therapeutic strategy, which we hope will provide improved patient access

ASX:**ALA**

arovella
THERAPEUTICS

Thank You

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