

**ASX Release**

30 January 2024

**AROVELLA ENHANCES SOLID TUMOUR PIPELINE BY LICENSING NOVEL CAR-iNKT CELL ARMOURING TECHNOLOGY**

- Arovella has entered into a global, exclusive license with University of North Carolina Lineberger Comprehensive Cancer Center to incorporate a novel armouring cytokine technology (IL-12-TM) for its CAR-iNKT cell platform
- Arovella is the only company globally developing IL-12-TM armoured CAR-iNKT cells
- This armouring cytokine technology:
  - results in a ten-fold increase in circulating CAR-iNKT cell numbers in animal models for solid tumours
  - significantly improved CAR-iNKT anti-tumour activity
  - significantly improved overall survival in animal models
  - enhances CAR-iNKT cells to potentially treat a range of solid tumour types
- Patent applications filed to protect the technology until at least 2043
- Investor webinar is scheduled for 11 am AEDT on Wednesday, 31<sup>st</sup> January. [Please register here.](#)

**MELBOURNE, AUSTRALIA 30 January 2024:** Arovella Therapeutics Ltd (ASX: ALA) has signed a global, exclusive License Agreement with the University of North Carolina Lineberger Comprehensive Cancer Center (UNC Lineberger) to incorporate UNC Lineberger’s novel IL-12-TM (cytokine technology) into Arovella’s CAR-iNKT cell therapy platform. The technology was developed by Professor Gianpietro Dotti, a pioneer of CAR-iNKT cells, and was recently published in the prestigious peer-reviewed journal Nature Communications.<sup>1</sup>

Arovella’s CEO and MD, Dr Michael Baker, commented: “We are incredibly excited to license the IL-12-TM technology from Professor Dotti’s laboratory for use with our CAR-iNKT cell platform. The data supporting solid tumours is compelling and will see Arovella enhance its solid tumour pipelines and effectiveness.”

Professor Dotti, a research professor at UNC and director of the Lineberger Comprehensive Cancer Center Immunotherapy Program, commented: “We have continued to make important advancements to use CAR-iNKT cells to treat various tumour types. What we have discovered by engineering CAR-iNKT cells to generate IL-12-TM is unexpected. We look forward to working with Arovella to test this exciting technology in clinical trials.”

The licence has no immediate material financial impact on the Company as a result of signing the agreement. There is no upfront fee payable for the license, and future licensing fees will include annual license maintenance fees, stage-gated, industry-standard development milestones for the first patient dosed in a pivotal clinical trial and marketing approval. The Licence also includes a low single-digit royalty on future sales. Further details on key license terms are included below.

The data demonstrates that IL-12-TM enhances CAR-iNKT cell persistence, cell number and antitumour activity in several animal cancer models including solid tumour cancers such as neuroblastoma. Arovella

<sup>1</sup> <https://www.nature.com/articles/s41467-023-44310-y>

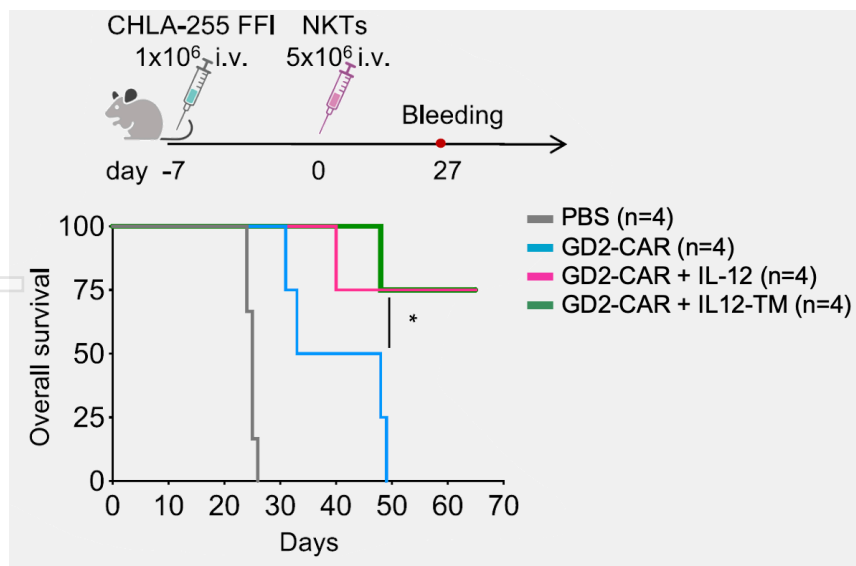
intends to incorporate the IL-12-TM technology into its solid tumour programs and will be the only iNKT cell company working with the technology.

IL-12-TM is a modified version of the human cytokine, interleukin 12 (IL-12). Due to bridging the innate and adaptive immunity and potentially stimulating the production of IFN- $\gamma$ , a cytokine coordinating natural mechanisms of anticancer defence, IL-12 was considered the ideal candidate for human tumour immunotherapy. However, side effects associated with systemic administration limited its use as a stand-alone therapeutic.

IL-12-TM has been modified to include a 'membrane anchor', which keeps the IL-12 attached to the CAR-iNKT cell and prevents it from circulating freely in the patient's bloodstream. This enables the IL-12-TM to have the desired effect on the CAR-iNKT cell and reduces the risk of off-target effects and toxicity.

When IL-12-TM is added to CAR-iNKT cells, it promotes the proliferation and survival of the CAR-iNKT cells. This means that when the CAR-iNKT cell comes in contact with a target tumour cell, it proliferates more, leading to higher numbers of CAR-iNKT cells. In addition, the cells do not get 'exhausted' as quickly and therefore survive longer, again contributing to higher CAR-iNKT cell numbers.

The IL-12-TM technology was tested in a mouse model of neuroblastoma, a cancer that can affect various regions of the central nervous system. When the number of CAR-iNKT cells was assessed in the mice four weeks after dosing, CAR-iNKT cells containing IL-12-TM were found at much higher numbers in the bloodstream (>10 times) than CAR-iNKT cells that did not contain IL-12. This correlated with substantially better antitumour activity and survival outcomes in the mice with approximately 75% of mice still alive 60 days after treatment for the IL-12-TM group while all mice in the group treated with CAR-iNKT cells lacking IL-12 had died (Figure 1).



**Figure 1.** CHLA-255 neuroblastoma cells were engrafted into mice before treatment with PBS, iNKT cells expressing a CAR to target GD2 lacking the cytokine technology (GD2-CAR), GD2 targeting iNKT cells with secreted IL-12 (GD2-CAR +IL-12) or GD2 targeting iNKT cells with a membrane anchored IL-12 (GD2-CAR + IL-12-TM). Landoni et al 2024, Nature Communications.

The full publication for the IL-12-TM data is available from the Nature Communications website and can be found here - <https://www.nature.com/articles/s41467-023-44310-y>.

### **Armouring CAR-iNKT cells to treat solid tumours**

Arovella's CAR-iNKT cells are being developed as an off-the-shelf solution for cancer treatment. They have inherent properties that may make them amenable to targeting solid tumours, such as

- (i) the ability to infiltrate tissues and tumours<sup>i,ii</sup>,
- (ii) the ability to block or kill cells that promote tumour survival such as myeloid-derived suppressor cells (MDSCs) and tumour-associated macrophages (TAMs),<sup>iii</sup> and
- (iii) the ability to release cytokines to stimulate an immune response and recruit other immune cells to target the tumour cells.<sup>iv,v</sup>

Armouring CAR-iNKT cells is one of Arovella's strategies to further enhance and differentiate its platform to tackle solid tumours. The intellectual property licensed from UNC Lineberger was filed in 2023 and covers use of the IL-12-TM in iNKT cells and the filed patent will provide protection until at least 2043. The data generated using the IL-12-TM armouring strategy demonstrates the promise of CAR-iNKT cells, and their potential utility across a range of tumour types.

IL-12-TM is expected to complement Arovella's CLDN18.2 program, recently licensed from Sparx Group. Arovella is developing the world's first CAR-iNKT cell therapy targeting CLDN18.2 to target gastric cancers (GC), gastroesophageal junction cancers (GEJC) pancreatic cancers (PC), and other solid tumours that express CLDN18.2. GC and GEJC continue to present as high unmet medical needs with over one million new cases diagnosed per annum globally and 789,000 deaths, making it the fourth most fatal cancer globally.<sup>vi</sup> Over 496,000 individuals were diagnosed with PC worldwide in 2020 with an estimated 466,000 deaths the same year.<sup>vii</sup> Stage 4 pancreatic cancer has a five-year survival rate of 1% with the average patient living for approximately 1 year after their diagnosis.<sup>viii</sup> The global gastric cancer market size was valued at \$2.1 billion in 2021, and is projected to reach \$10.7 billion by 2031, growing at a CAGR of 17.9% from 2022 to 2031.<sup>ix</sup>

In addition, Arovella continues to work with Imugene combining its oncolytic virus platform, CF33, with ALA-101. Incorporating IL-12-TM may provide improved activity against a range of solid tumours for this collaboration.

### **Differentiation of Arovella's CAR-iNKT cell platform**

Arovella will be the only CAR-iNKT cell company developing products incorporating this cytokine. The IL-12-TM cytokine technology was also compared to IL-15, another cytokine that has been used to enhance persistence of iNKT cells. IL-15 has been used by other groups to enhance the antitumor activity of CAR-iNKT cells against neuroblastoma. When compared directly with IL-15 in a mouse model of neuroblastoma, CAR-iNKT cells incorporating IL-12-TM displayed significantly improved antitumour activity. For mice treated with CAR-iNKT cells incorporating IL-15, 100% of the animals had succumbed to the cancer cells by day 42. In contrast, 80% of the mice treated with IL-12-TM containing CAR-iNKT cells were alive after 60 days, when the experiment was completed.

### Key terms of the licence agreement

The licence has no immediate material financial impact on the Company as a result of signing the agreement, which has no conditions precedent and is effective immediately. The preclinical data published in Nature Communications provides the proof-of-concept studies to demonstrate the potential of the technology. The next step is to integrate IL-12-TM into Arovella's existing programs and is not expected to materially increase the costs of these programs<sup>2</sup>.

In lieu of an upfront license fee, Arovella will enter into a sponsored research agreement (SRA) and a clinical trial agreement (CTA) with Professor Dotti's lab, to be negotiated at a later date. The license includes industry-standard stage-gated milestone payments for (i) the first patient dosed in a pivotal clinical trial and (ii) marketing approval of a product incorporating the technology for the first two products. Total milestone fees payable under the license agreement total US\$10 million. Future license payments also include annual license maintenance fees and low single-digit royalties associated with commercial sales of the approved products.

The timing of the cash milestones is contingent on pre-clinical development success and, thereafter, clinical trial success. The majority of the contingent cash milestone payments are due upon market approvals. Accordingly, and based on other therapeutic drug development programs, this would typically be longer than seven years, hence the timing of such payments are indeterminable.

The Licence Agreement contains standard termination provisions, and there are no associated termination fees. The Agreement shall expire at the latest of (i) expiration of the last to expire patent included in the Patent Rights, (ii) the expiration of any market exclusivity relating to a Licensed Product, or (iii) ten (10) years from the first commercial sale of a Licensed Product.

### Investor webinar

Dr Michael Baker will hold an investor webinar for shareholders and interested parties to discuss this announcement and development for Arovella.

**Time:** 11am AEDT

**Date:** Wednesday 31 January 2024

**Registration:** [https://us02web.zoom.us/webinar/register/WN\\_ZTCz-0DMS5W22Qi8\\_bbkpw](https://us02web.zoom.us/webinar/register/WN_ZTCz-0DMS5W22Qi8_bbkpw)

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

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

Questions can be submitted on the day or sent in advance to [investor@arovella.com](mailto:investor@arovella.com).

*Release authorised by the Board of Directors of Arovella Therapeutics Limited.*

<sup>2</sup> <https://www.nature.com/articles/s41467-023-44310-y>

**ASX: ALA**

Arovella Therapeutics Limited  
ACN 090 987 250



**Dr Michael Baker**

**Chief Executive Officer & Managing Director**

**Arovella Therapeutics Ltd**

Tel +61 (0) 403 468 187

investor@arovella.com

**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  $\alpha$ -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;  **$\alpha$ GalCer** – 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](http://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.

---

<sup>i</sup> <https://pubmed.ncbi.nlm.nih.gov/29967365/>

**ASX: ALA**

Arovella Therapeutics Limited  
ACN 090 987 250

---

<sup>ii</sup> <https://pubmed.ncbi.nlm.nih.gov/33046868/>

<sup>iii</sup> <https://pubmed.ncbi.nlm.nih.gov/19411762/>

<sup>iv</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4517377/>

<sup>v</sup> <https://doi.org/10.4049/jimmunol.163.9.4647>

<sup>vi</sup> [https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(22\)00134-1/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(22)00134-1/fulltext)

<sup>vii</sup> <https://acsjournals.onlinelibrary.wiley.com/doi/10.3322/caac.21660>

<sup>viii</sup> <https://www.hopkinsmedicine.org/health/conditions-and-diseases/pancreatic-cancer/pancreatic-cancer-prognosis>

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

For personal use only





# Exclusive Global License

IL-12-TM cytokine technology from  
University of North Carolina Lineberger  
Comprehensive Cancer Center

January 2024



ersonal use only

# 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. Past performance information given in this presentation is given for illustrative purposes only and should not be relied upon as (and is not) an indication of future performance. The presentation includes forward-looking statements regarding future events and the future financial performance of Arovella. Forward looking words such as “expect”, “should”, “could”, “may”, “predict”, “plan”, “will”, “believe”, “forecast”, “estimate”, “target” or other similar expressions are intended to identify forward-looking statements. Any forward looking statements included in this document involve subjective judgment and analysis and are subject to significant uncertainties, risks and contingencies, many of which are outside the control of, and are unknown to, Arovella and its officers, employees, agents or associates. In particular, factors such as outcomes of clinical trials and regulatory decisions and processes may affect the future operating and financial performance of Arovella. This may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. The information also assumes the success of Arovella’s business strategies. The success of the strategies is subject to uncertainties and contingencies beyond control, and no assurance can be given that the anticipated benefits from the strategies will be realised in the periods for which forecasts have been prepared or otherwise. Given these uncertainties, you are cautioned to not place undue reliance on any such forward looking statements. Arovella is providing this information as of the date of this presentation and does not assume any obligation to update any forward-looking statements contained in this document as a result of new information, future events or developments or otherwise.
4. 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.
5. 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.
6. Any opinions expressed reflect the Company’s position at the date of this presentation and are subject to change.
7. 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. The distribution of this presentation in jurisdictions outside Australia may be restricted by law and any such restrictions should be observed.



# 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, potential treatment for CD19+ blood cancers, 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 broaden its applications

## Unique value proposition

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



# iNKT cells to target solid tumours

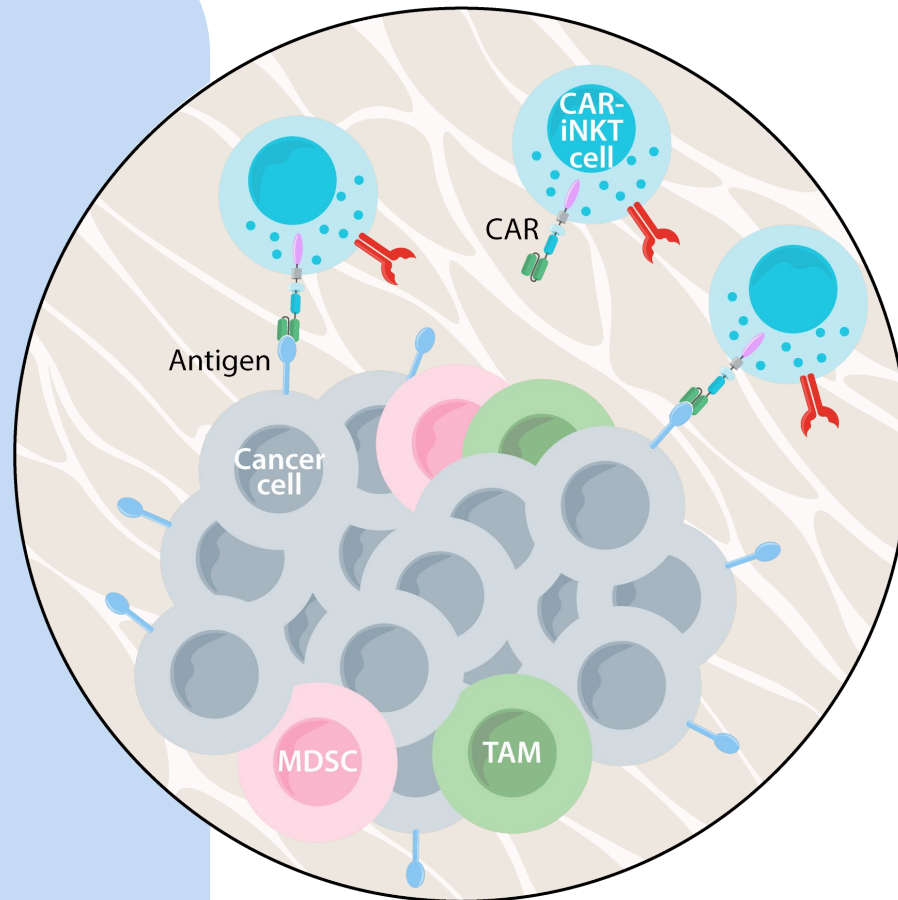
Arovella is implementing its strategy to target and kill solid tumours – 90% of newly diagnosed cancer cases<sup>1</sup>

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

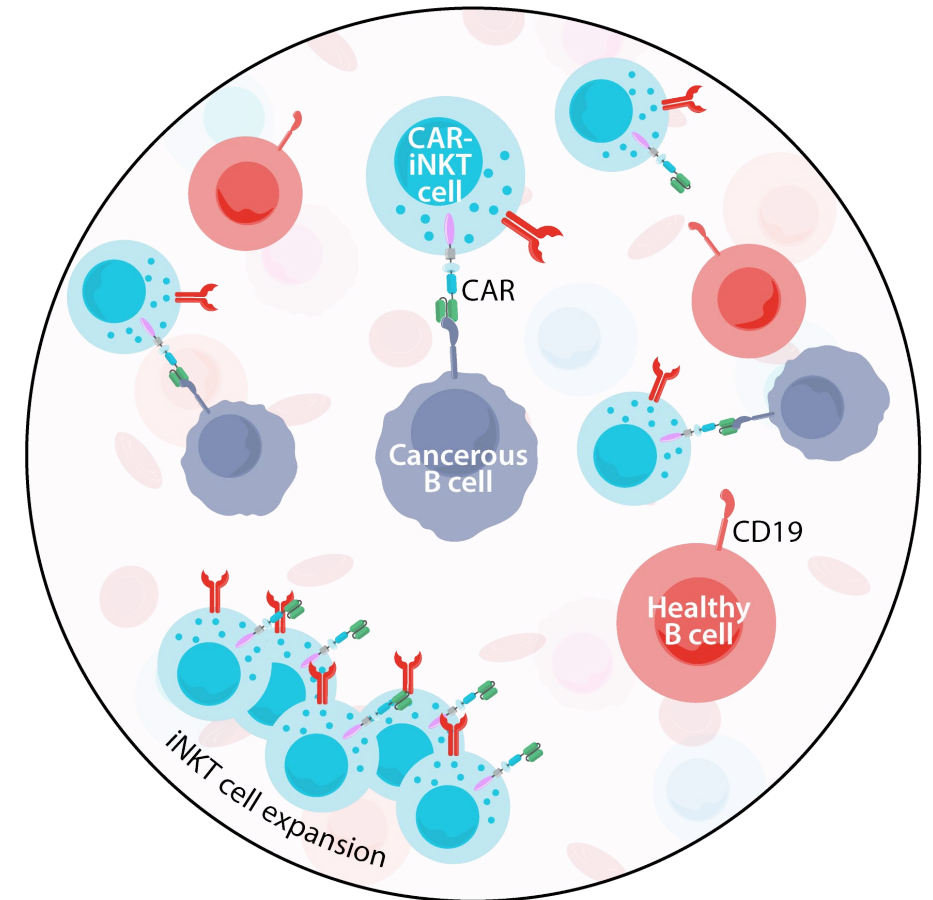
# Solid tumours pose challenges to cell therapies



Solid tumours are more **difficult to treat with cell therapies**



**Solid tumour**



**Blood cancer**



Access to tumour



Antigen specificity and uniformity

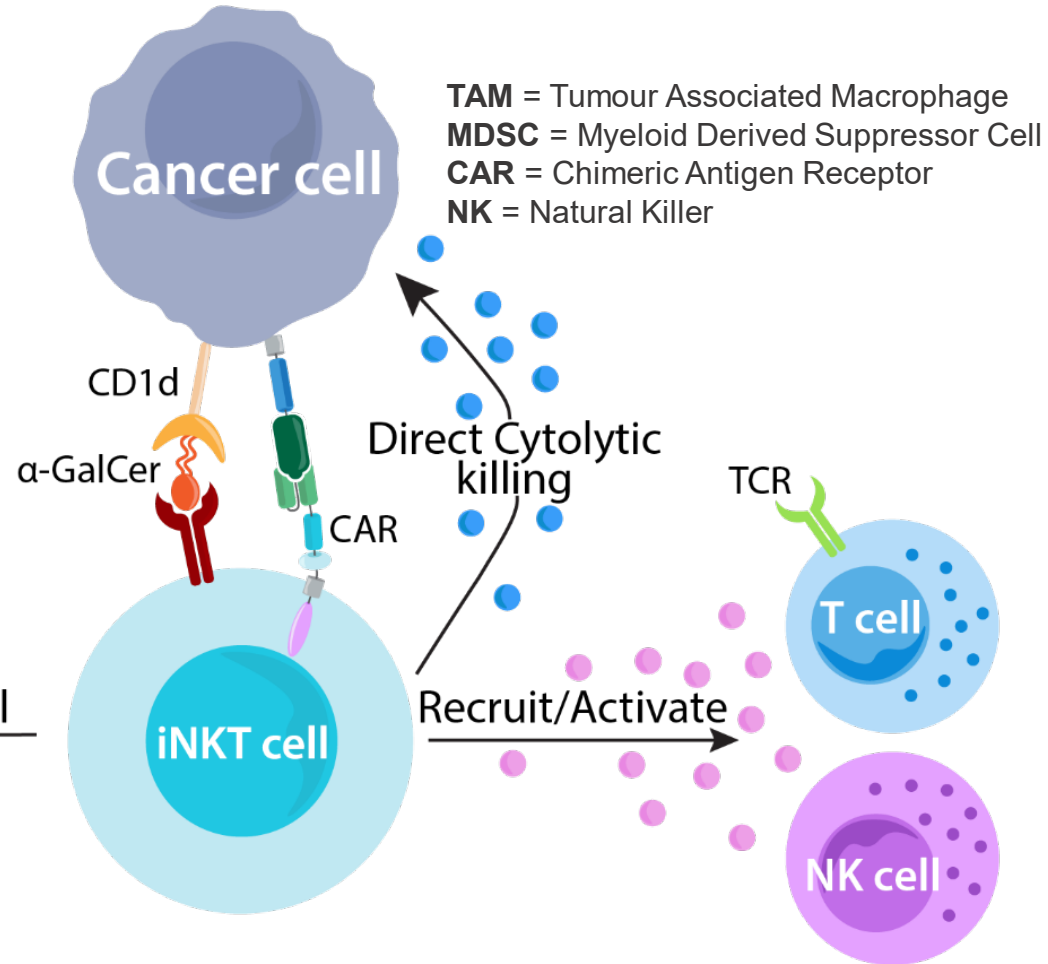


Tumour microenvironment contains cells that support cancer cell growth



# iNKT cells to combat solid tumours

iNKT cells have several properties to attack solid tumours



Modification  
of the tumour  
microenvironment

## iNKT cells

- Home to tissues and infiltrate tumours<sup>1,2</sup>
- Block or kill cells that promote tumour growth<sup>3</sup>
- Recruit other immune cells that can also kill tumour cells<sup>4,5</sup>

1. Crosby and Kronenberg 2018 Nat Rev Immuno - 10.1038/s41577-018-0034-2; 2. Heczey et al., 2020 Nature Medicine - 10.1038/s41591-020-1074-2; 3. Song et al., 2009 J Clin invest - 10.1172/JCI37869; 4. Gottschalk et al., 2015 Front Immunol - 10.3389/fimmu.2015.00379; 5. Carnaud et al., 1999 J Immunol - 10.4049/jimmunol.163.9.4647

# 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 CAR-iNKT cells with novel armouring technologies



## Create unique partnerships

Create partnerships to use novel combination therapies with synergistic effects



# 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 CAR-iNKT cells with novel armouring technologies



## Create unique partnerships

Create partnerships to use novel combination therapies with synergistic effects



# Introducing Interleukin 12 (IL-12)

IL-12 is a cytokine that has been well studied for immunotherapy

## Cytokines for Cancer Treatment

**1986**

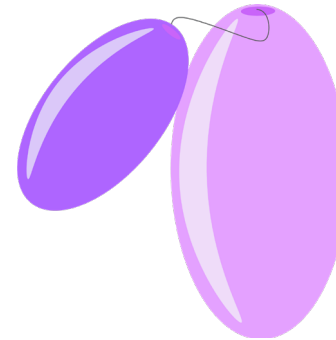
First cytokine approved to treat cancer

**>40 cytokines** studied in preclinical and clinical trials

**2 cytokines** approved as single agents to treat cancer

Cytokines can provide “armouring” to cell therapies, enhancing their anti-tumour activity

## IL-12



- Potent, pro-inflammatory cytokine with diverse functions
- Increases activation and cell killing capacity of T and NK cells
- Inhibits or reprograms immunosuppressive cells, such as TAMs and MSDCs
- Has demonstrated strong antitumor effects in preclinical studies
- Unwanted toxicity has limited its success as a monotherapy

# “Armouring” CAR-iNKT cells

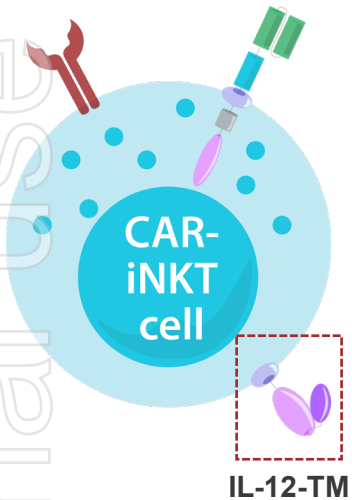
IL-12-TM (cytokine technology) enhances CAR-iNKT cell activity in solid tumours

## 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 and 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 to integrate IL-12-TM into CAR-iNKT cell platform

Exclusive, global licence with UNC Lineberger Comprehensive Cancer Center



LINEBERGER  
COMPREHENSIVE  
CANCER CENTER

**Exclusive global licence with UNC Lineberger Comprehensive Cancer Center**

to use the IL-12-TM construct in CAR-iNKT cells



**Attractive fee structure**

modest short-term capital requirements



**Industry-standard milestones**

payable in cash and low single digit royalties

IL-12-TM technology

TARGET SOLID TUMOURS

CAR-iNKT cell therapy platform

Arovella will combine the IL-12-TM technology with its iNKT cell therapy platform to target solid tumours

**Many solid tumours are high priority targets of unmet need**



The licence strengthens Arovella's **exciting programs targeting** solid tumours, leveraging its manufacturing progress for ALA-101



IL-12-TM enhances CAR-iNKT cell activity against neuroblastoma

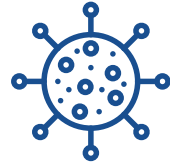
First CAR-iNKT cell product  
**expressing IL-12-TM**

# The Inventor – Professor Gianpietro Dotti, M.D., Ph.D.

A renowned world expert on CAR-iNKT cells



UNIVERSITÀ  
DEGLI STUDI  
DI MILANO



- CAR-iNKT cell pioneer, created the first CAR-iNKT cell construct
- Leading authority on CAR-T and CAR-iNKT cells
- Developed CAR-based strategies to target neuroblastoma in pediatric patients



- Medical Degree from the University of Milan, Italy
- Clinical Training and Board certification in Hematology (University of Parma)
- Post doctoral fellowship in translation research (Center for Cell and Gene Therapy at the Baylor College of Medicine)



- Research Professor of Microbiology and Immunology at UNC
- Director of the Cellular Immunotherapy Program at Lineberger Comprehensive Cancer Center at UNC



- More than 200 peer-reviewed research articles
- Received the Highly Cited Researchers (Top 1%) award from Web of Science, Clarivate Analytics, in 2020, 2021, 2022, 2023.

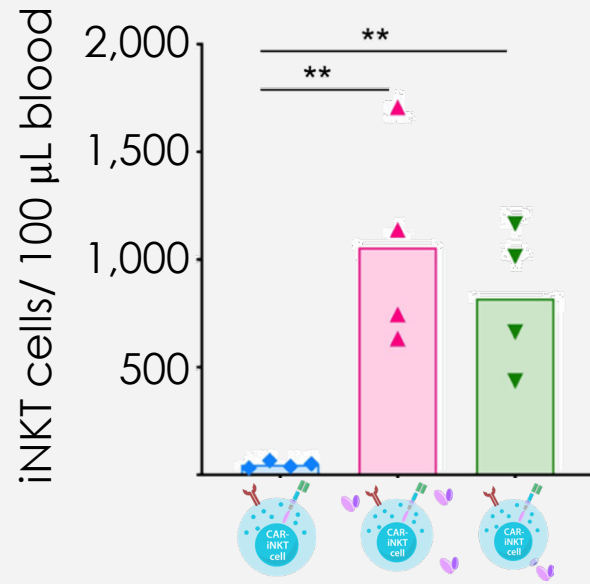
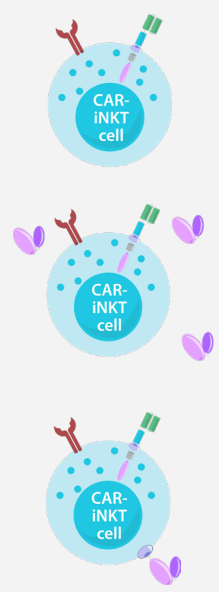
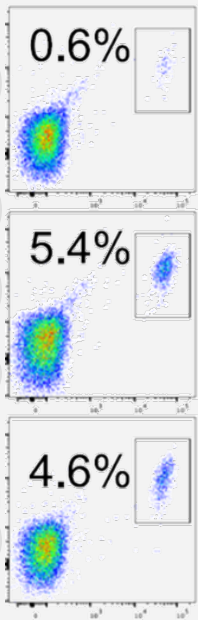


# Key benefits of IL-12-TM for CAR-iNKT cells

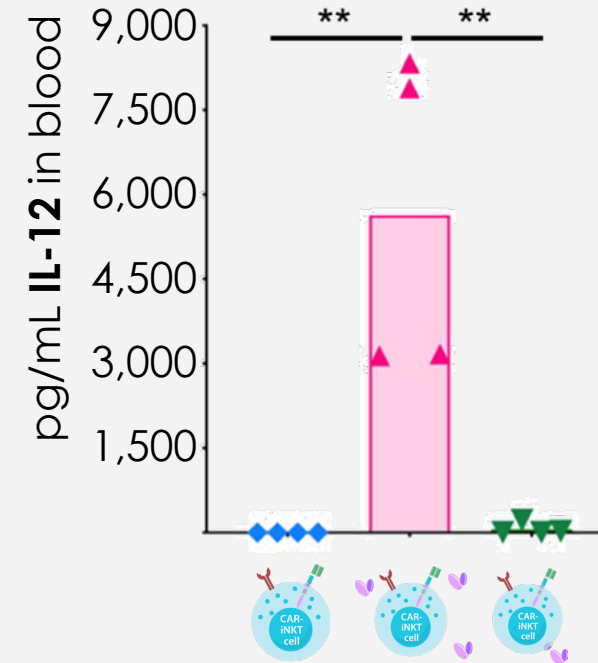
IL-12-TM increases CAR-iNKT cell numbers and does not get released into the bloodstream



## Increased CAR-iNKT cell numbers



## IL-12-TM is not released from CAR-iNKT cells



Landoni et al., Nature Communications (2024)

# Key benefits of IL-12-TM for CAR-iNKT cells

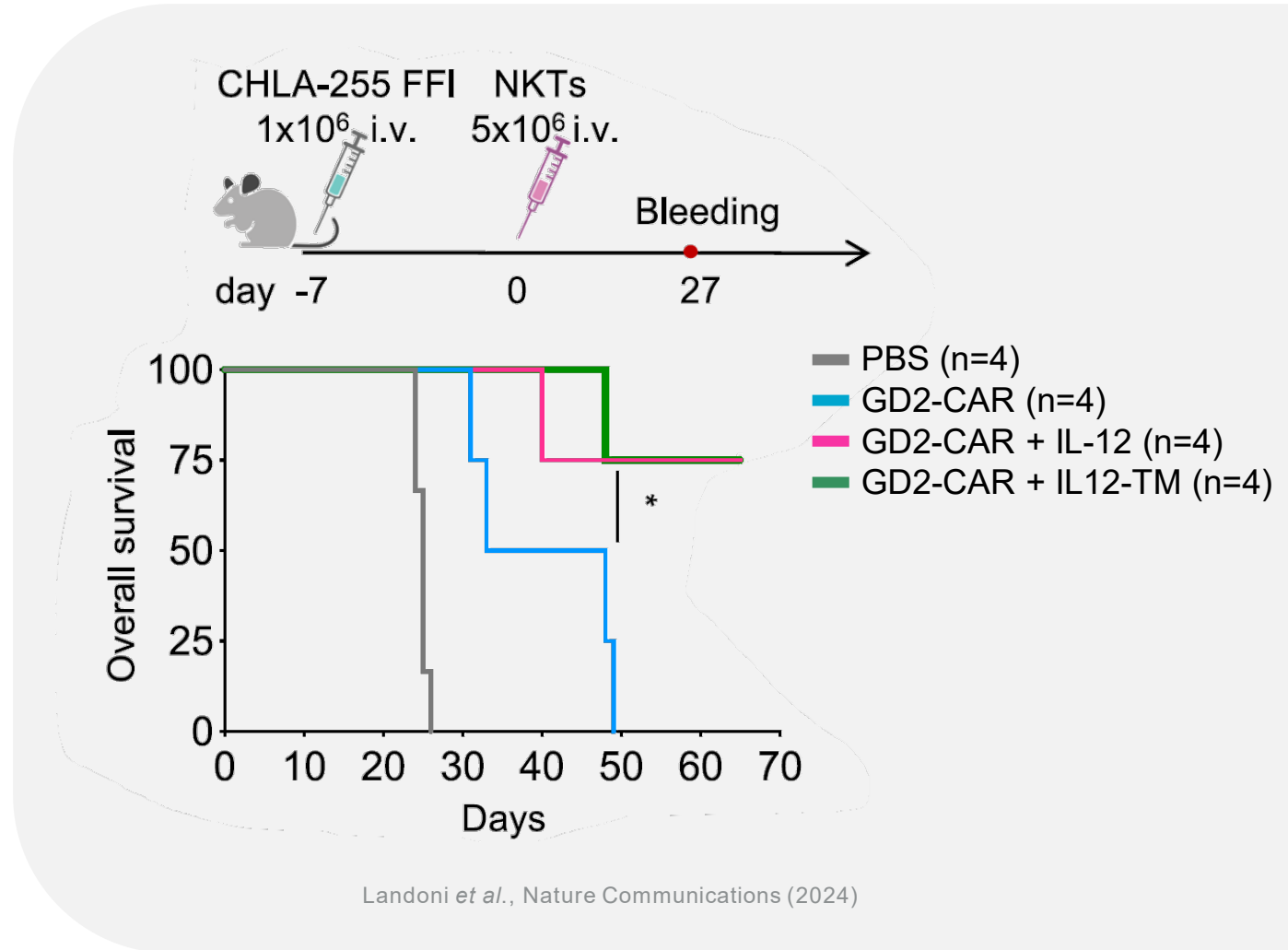
IL-12-TM enhances antitumor activity of CAR-iNKT cells

- Tumour cells expressing GD2 and were intravenously delivered into mice before treatment with CAR-iNKT cells

- Mice were treated with:

- PBS (saline)
- GD2-CAR
- GD2-CAR + IL-12
- GD2-CAR + IL-12-TM

- After 60 days, only mice treated with GD2-CAR + IL12 or IL-12-TM remained alive



# Key benefits of IL-12-TM for CAR-iNKT cells

We expect IL-12-TM to enhance Arovella's CAR-iNKT cell platform



## Increases CAR-iNKT cell numbers

IL-12-TM prolongs persistence of CAR-iNKT cells. Cells continue to proliferate and increase in number.



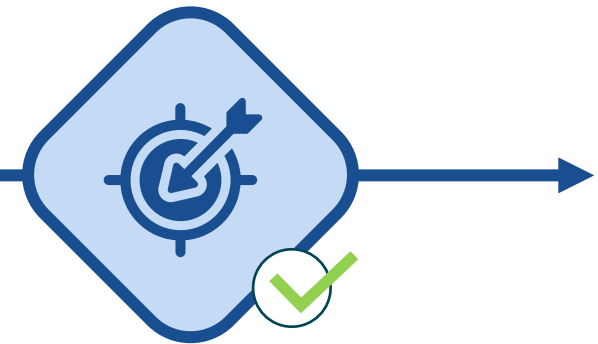
## IL-12-TM is not released from CAR-iNKT cells

First CAR-iNKT cell product with membrane-anchored IL-12. IL-12-TM is not released from the cells and is expected to be safer.



## Enhances CAR-iNKT cell antitumour activity

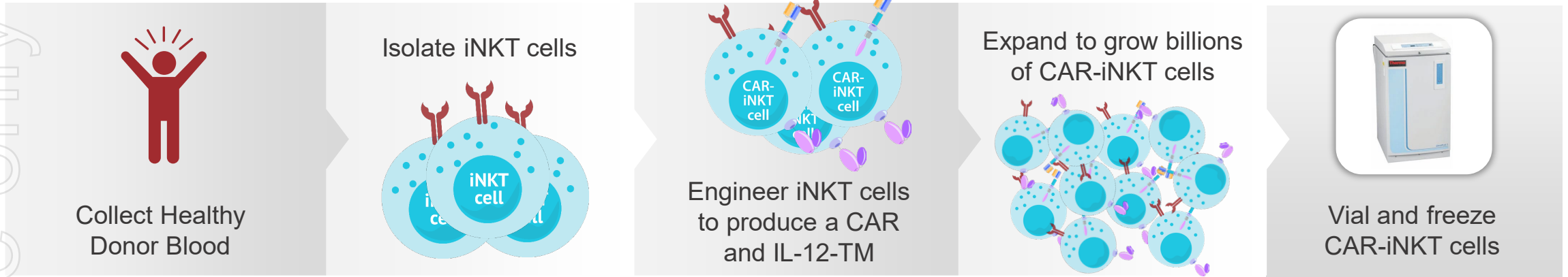
IL-12-TM enhances CAR-iNKT antitumor activity against solid tumour cancers like neuroblastoma



# Manufacturing CAR-iNKT cells to express IL-12-TM

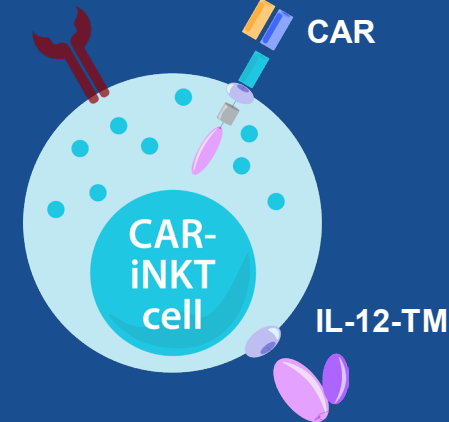
Integration of IL-12-TM will leverage Arovella's existing manufacturing process

## MANUFACTURING



Arovella will use its **proprietary manufacturing process**

to create CAR-iNKT cells incorporating IL-12-TM



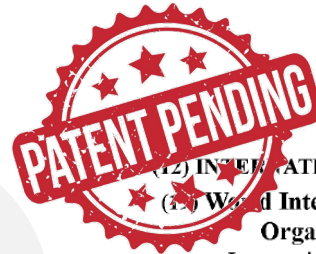
# Robust intellectual property

Filed patent to provide patent protection until at least 2043

Composition of matter claims for a unique IL-12-TM sequence

National phase to be filed in major jurisdiction, including US, Europe, China, Japan, South Korea and Australia

Arovella is the only Company combining CAR-iNKT cells with IL-12



(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(21) World Intellectual Property Organization  
International Bureau

(43) International Publication Date  
03 August 2023 (03.08.2023)



(10) International Publication Number  
**WO 2023/147564 A2**

(51) International Patent Classification:  
C12N 15/85 (2006.01) A61K 35/14 (2015.01)

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(21) International Application Number:  
PCT/US2023/061600

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

(22) International Filing Date:  
30 January 2023 (30.01.2023)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
63/304,556 28 January 2022 (28.01.2022) US

(71) Applicant: THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL [US/US]; 109 Church Street, Chapel Hill, NC 27516 (US).

Published:

— without international search report and to be republished upon receipt of that report (Rule 48.2(g))

(72) Inventors: DOTTI, Gianpietro; 111 Quailview Drive, Chapel Hill, NC 27516 (US). LANDONI, Elisa; 496 Melanie Ct, Chapel Hill, NC 27514 (US). SAVOLDO, Barbara; 111 Quailview Drive, Chapel Hill, NC 27516 (US).

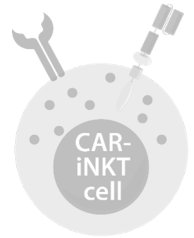
(74) Agent: BRYAN, Erin, E.; Morse, Barnes-Brown & Pendleton, P.C., CityPoint, 480 Totten Pond Road, 4th Floor, Wilmington, NC 28403 (US).



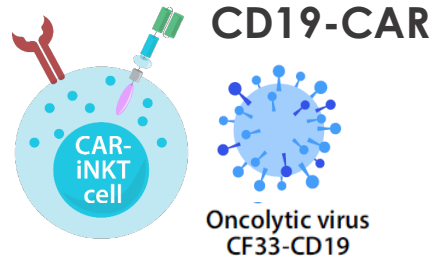


# IL-12-TM to enhance Arovella's solid tumour strategies

Arovella is developing several solid tumour strategies that will leverage the technology

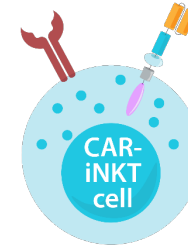


CD19-CAR



CD19-CAR

Oncolytic virus  
CF33-CD19



Novel Targets

Introduction of CLDN18.2

ALA-101

ALA-101 + onCARlytics

CLDN18.2

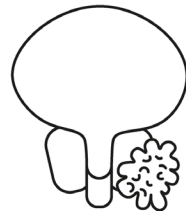
IL-12-TM



Non-Hodgkin's  
Lymphoma



Head and  
Neck Cancer



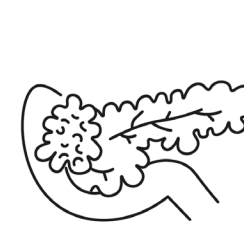
Prostate  
Cancer



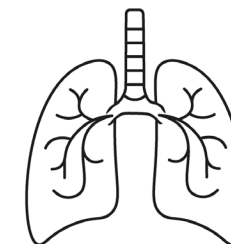
Brain  
Malignancies



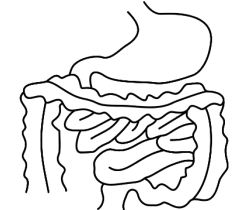
Triple negative  
breast cancer



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 submission 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*

# Financial overview

## Financial Snapshot

ASX CODE	ALA
Market capitalisation <sup>1</sup>	\$119.39 million
Shares on issue	918.4 million
52-week low / high <sup>1</sup>	\$0.025 / \$0.155
Cash Balance (December 31 2023)	\$4.76 million

## Major Shareholders

Shareholder	Ownership (%) <sup>1</sup>
THE TRUST COMPANY (AUSTRALIA) LIMITED	55,613,086 (6.16%)
RICHARD JOHN MANN	50,905,657 (5.64%)
UBS NOMINEES PTY LTD	20,620,196 (2.29%)
BLACKBURNE CAPITAL PTY LTD	17,637,456 (1.96%)
DYLIDE PTY LTD	15,666,666 (1.74%)

<sup>1.</sup> As of 29 January 2024

## ALA Price and Volume - 12 Months<sup>1</sup>



# 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

## CAR-iNKT cells have multiple anticancer properties

CAR-iNKT cells are dual-targeting with enhanced cancer killing ability

## Improved manufacturing logistics

Allogeneic CAR-iNKT cells will significantly improve logistics and increase patient access



## 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

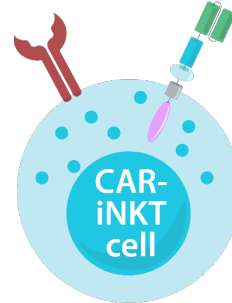
## iNKT cells have properties that may assist targeting solid tumours

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

## Arovella is expanding its pipeline

Arovella has added a novel CLDN18.2 CAR and IL-12-TM to its platform, to target solid tumours

# Arovella's CAR-iNKT Cell Platform



ASX:ALA



**Thank You**

**Dr. Michael Baker**

CEO & Managing Director

Email: [investor@arovella.com](mailto:investor@arovella.com)

Mobile: +61 403 468 187



ersonal use only



# Investor Webinar



**Dr. Michael Baker**  
CEO & MANAGING  
DIRECTOR

**DATE: Wed, 31 Jan 2024**

**TIME: 11:00 AM (AEDT)**

[Please register here](#)

