ASX Release

20 April 2026

AROVELLA PRESENTS POSTER AT AACR ANNUAL MEETING

Highlights:

- **Arovella presents its recent CLDN18.2 pre-clinical data at the American Association for Cancer Research (AACR) Annual Meeting in San Diego.**
- **Data shows CLDN18.2 CAR-iNKT cells effectively kill CLDN18.2-positive pancreatic cancer and gastric cancer cells in in vitro studies**

MELBOURNE, AUSTRALIA 20 April 2026: Arovella Therapeutics Ltd (ASX: ALA), a biotechnology company focused on developing its invariant Natural Killer T (iNKT) cell therapy platform, is pleased to announce that today it will be presenting a poster describing its CAR-iNKT cell therapy targeting CLDN18.2-positive cancers at the American Association for Cancer Research (AACR) Annual Meeting in San Diego. The AACR annual meeting is a focal point of the cancer research community, where scientists, clinicians, other health care professionals, survivors, patients, and advocates gather to share the latest advances in cancer science and medicine.

The poster, titled *Allogeneic CAR-iNKT cell therapy targeting CLDN18.2-positive gastric and pancreatic cancers* describes in detail the data that was released in Arovella's announcement on 1 April 2026, CLDN18.2 CAR iNKT Cell Preclinical Data Update.

Arovella CEO and Managing Director, Dr Michael Baker, commented: "We are delighted to have been accepted to present our CLDN18.2-CAR-iNKT cell data at the AACR conference. It is exciting data and highlights the impressive performance of the CLDN18.2 CAR and the additional benefit of incorporating Arovella's cytokine armouring technology, IL-12-TM. We are looking forward to generating additional data in due course."

A recent video with Dr Baker's explanation of the data can be viewed here.

A copy of the poster is attached to this release and is available on our website at https://www.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
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'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 glycolipid bound CD1d, another antigen found on the surface of several cancer types. ALA-101 has had its IND accepted by the US FDA and is being developed as an allogeneic cell therapy, which means it can be given from a healthy donor to a patient. Arovella is also expanding into solid tumour treatment through its CLDN18.2-targeting technology licensed from Sparx Group. Arovella will also incorporate its IL-12-TM technology into its solid tumour programs.

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.

Allogeneic CAR-iNKT cell therapy targeting CLDN18.2-positive gastric and pancreatic cancers

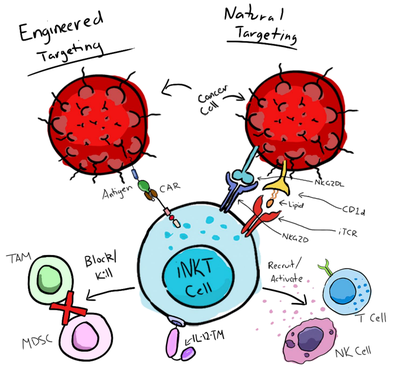
Clinton Heinze[1,2], Elisa Landoni[2], Michelle Ferguson[1], Nicole Van Der Weerden[1], Robson Dossa[1], Simon Poon[1], Kelvin Yip[1], Jacqui Cumming[1], Alfie Baker[1], Sarah Sandford[1], Michael Baker[1], Barbara Savoldo[2], Gianpietro Dotti[2]

[1] **Arovella Therapeutics Ltd,** Victoria, Australia
[2] **Lineberger Comprehensive Cancer Centre**, University of North Carolina Chapel Hill, United States

#140

CAR-iNKT cells: An allogeneic, multimodal anti-tumour platform enabling superior and rapid activity relative to CAR-T cells

- Invariant Natural Killer T (iNKT) cells are a unique subset of unconventional T cells that naturally target and kill cancer cells[1].
- iNKT cells bridge adaptive and innate immune responses; they express a semi-invariant TCR (iTCR) that recognises glycolipids presented by the monomorphic, MHC-like molecule CD1d[2]; they also express NKG2D to recognise and kill tumour cells via NKG2D ligands.
- Engineering iNKT cells with a Chimeric Antigen Receptor (CAR) can create up to three complementary tumour targeting mechanisms, enhancing cytotoxicity[3].
- iNKT cells can be administered off-the-shelf without the risk of graft-versus-host disease (GvHD)[4], circumventing the need to knock out the endogenous TCR for an allogeneic cell therapy[5].
- CAR-iNKT cells have demonstrated superior efficacy to CAR-T cells in several in vivo tumour models[3,6,7].
- Cytokine armouring with IL-12 has been shown to enhance CAR-iNKT activity and engineering it to be tethered in membrane-bound form reduces toxicity risk.[8,9]



Multiple killing mechanisms of CAR-iNKT cells

1 **Via the CAR**
scFv is specific to tumour antigen target depending on tumour type

2 **Via the NKG2D pathway**
NKG2D ligands are upregulated in cancer cells

3 **Via lipid-bound CD1d**
Several cancers naturally express CD1d

TAM, Tumour Associated Macrophage; **MDSC,** Myeloid Derived Suppressor Cell; **NK,** Natural Killer

CLDN18.2-directed CAR-iNKT cells were generated to target gastric and pancreatic cancers

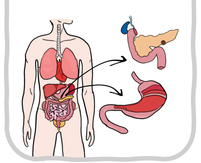
CLDN18.2 is a tight junction protein that is **not present in most healthy tissues**

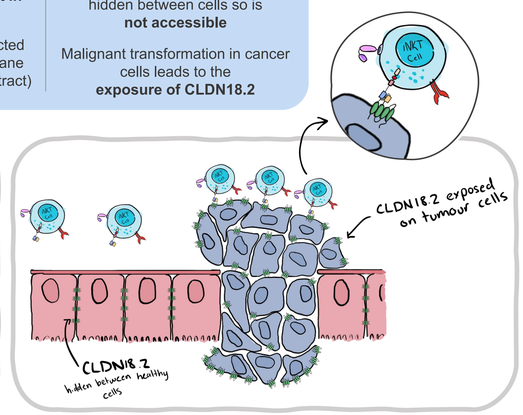
Expression is tightly restricted to gastric mucosal membrane epithelial cells (lining of GI tract)

In normal tissue CLDN18.2 is sequestered in tight junctions and hidden between cells so is **not accessible**

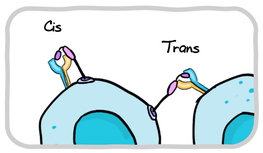
Malignant transformation in cancer cells leads to the **exposure of CLDN18.2**

CLDN18.2 is a prevalent target expressed by gastric and pancreatic cancers, in both primary lesions and metastases





iNKT cells armoured with membrane-anchored IL-12 (IL-12-TM)

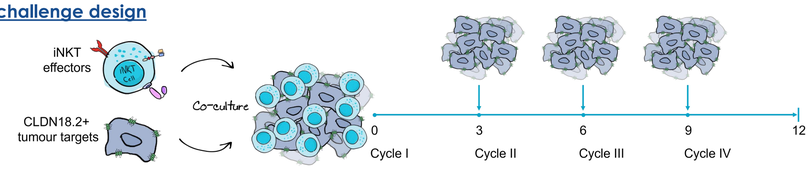


Tethering IL-12 to iNKT cells reduces the toxicity potential relative to exogenous co-administration or secretion of untethered IL-12

IL-12-TM can stimulate CAR-iNKT cells in **cis** (stimulation of self) and in **trans** (stimulation of other iNKT cells or endogenous immune cells)

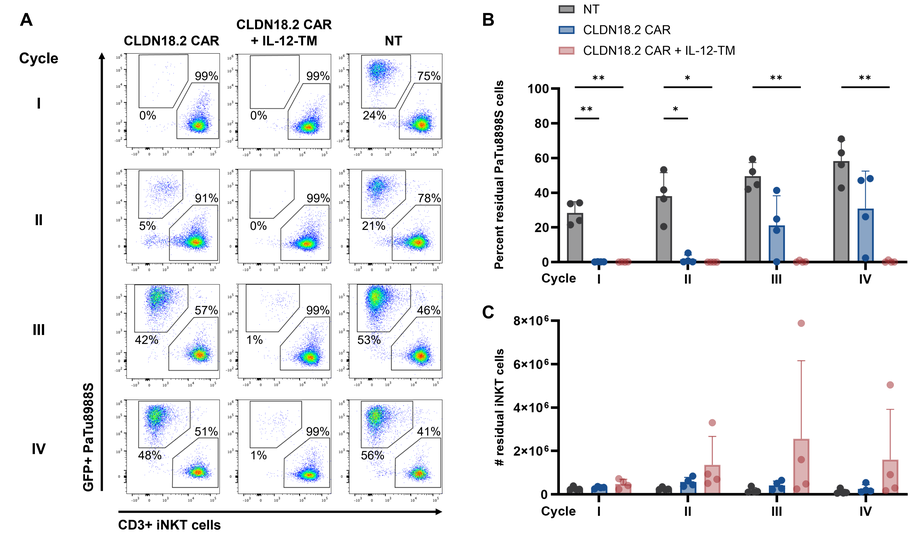
CLDN18.2-directed CAR-iNKT cells have potent cytotoxicity against tumour target cell lines and IL-12-TM enhances their expansion and persistence

Re-challenge design

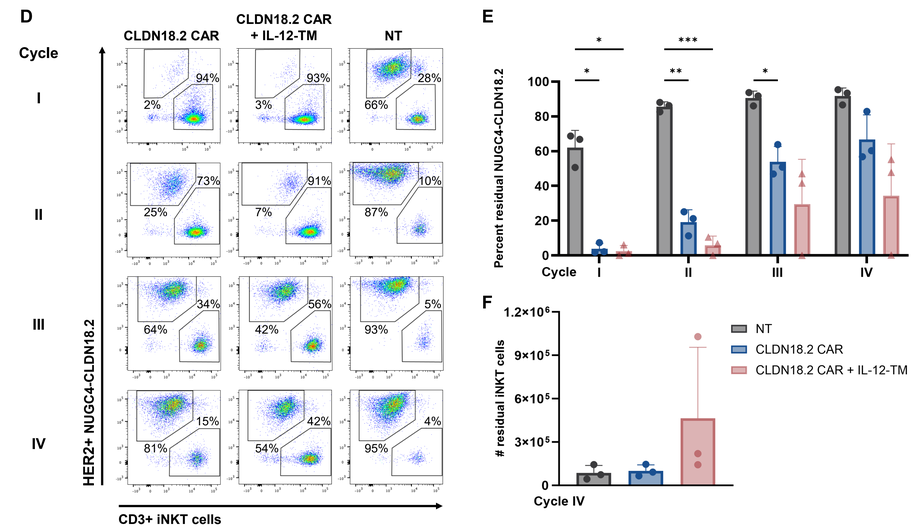


iNKT cells were co-cultured at a 1:1 CAR+ E:T ratio (PaTu8988S) or 1:2 CAR+ E:T ratio (NUGC4-CLDN18.2) with CLDN18.2+ tumour targets in four parallel wells. At the end of each three-day cycle, one well is harvested, and effector cells in remaining wells were re-seeded with new target cells. Wells were filled to 2 mL total volume with cytokine-free media.

Pancreatic cancer target - PaTu8988S



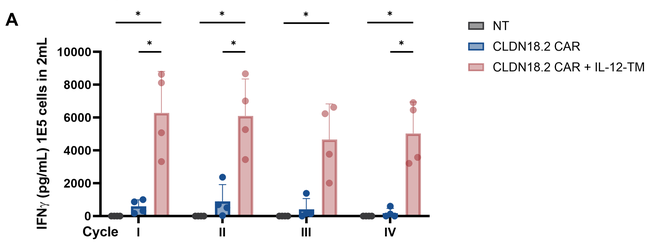
Gastric cancer target – NUGC4-CLDN18.2



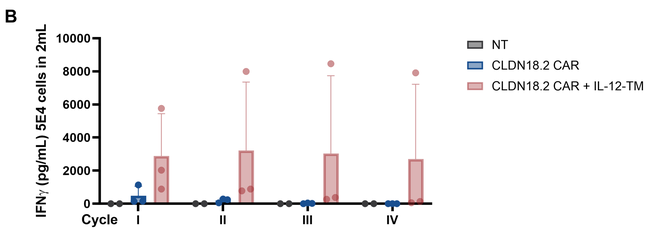
*(A) Representative flow plots of four donors; Summary of the quantification of (B) residual GFP+ PaTu8988S tumour cells and (C) CD3+ iNKT cells after each cycle when co-cultured at a 1:1 CAR+ E:T ratio. (D) Representative flow plots of three donors; Summary of the quantification of (E) residual HER2+ NUGC4-CLDN18.2 tumour cells and (F) CD3+ iNKT cells after Cycle IV only when co-cultured at a 1:2 CAR+ E:T ratio. Results show significant tumour control of both pancreatic and gastric tumour types with CAR-iNKT cells compared with non-transduced (NT) negative control effectors. Non-significant trends indicate iNKT cell expansion is enhanced with the inclusion of IL-12-TM. * p<0.05, ** p<0.005, *** p<0.0005. 2-way ANOVA with Tukey multi-comparisons and a Geisser-Greenhouse correction. Mean +/- SD is shown.*

IL-12-TM enhances IFNγ secretion by CAR-iNKT cells in the presence of tumour targets

PaTu8988S targets



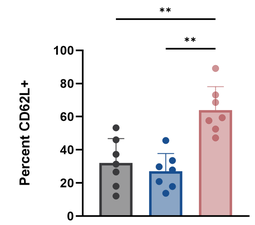
NUGC4-CLDN18.2 targets



*Quantification of IFNγ produced by non-transduced (NT), CLDN18.2 CAR, and CLDN18.2 CAR + IL-12-TM iNKT cells after each cycle for **(A)** PaTu8988S and **(B)** NUGC4-CLDN18.2 re-challenge co-cultures. Supernatants were harvested 24 hours after the initiation of each cycle. * p<0.05. 2-way ANOVA with Tukey multi-comparisons and a Geisser-Greenhouse correction. Mean +/- SD is shown.*

CAR-iNKT cells have phenotypic characteristics tied to persistent and potent anti-tumour cytotoxicity

IL-12-TM drives upregulated expression of memory marker, CD62L



For iNKT cells, higher CD62L expression has been linked with[9]:

1 **Improved cell expansion**
2 **Improved cell persistence**
3 **Enhanced anti-tumour activity**

*Prior to the initiation of the re-challenge experiment, CD62L expression was analysed in each donor. Results indicate upregulated CD62L expression with the inclusion of IL-12-TM (** p<0.005).*

1. Crowe *et al.*, 2002. doi: 10.1084/jem.20020092
2. Borg *et al.*, 2007. doi: 10.1038/nature05907
3. Rotolo *et al.*, 2018. doi: 10.1016/j.ccell.2018.08.017
4. Mavers *et al.*, 2017. doi: 10.3389/fimmu.2017.00900
5. Lv *et al.*, 2023. doi: 10.3389/fimmu.2023.1199145
6. Zhou *et al.*, 2024. doi: 10.1038/s43018-024-00830-0
7. Simonetta *et al.*, 2021. doi: 10.1158/1078-0432.CCR-21-1329
8. Kobayashi *et al.*, 1989. doi: 10.1084/jem.170.3.827
9. Landoni *et al.*, 2024. doi.org/10.1038/s41467-023-44310-y

Key Findings

- CLDN18.2-directed CAR-iNKT cells effectively control PaTu8988S pancreatic and NUGC4-CLDN18.2 gastric tumour growth after multiple challenges in vitro.
- Incorporation of membrane-anchored IL-12-TM drives upregulation of memory marker, CD62L, in unstimulated iNKT cells.
- Co-expression of IL-12-TM enhances CAR-iNKT cell expansion in the presence of CLDN18.2+ tumour targets.
- The inclusion of IL-12-TM significantly enhances IFNγ secretion by iNKT cells over numerous re-challenge cycles.
- Arovella's cytokine armoured CLDN18.2-directed CAR-iNKT cell product (ALA-105) is being developed for the treatment of CLDN18.2+ gastric and pancreatic cancers.
- Arovella's lead candidate, ALA-101, an allogeneic CD19-directed CAR-iNKT cell product has secured IND acceptance and is progressing to a phase I clinical trial for the treatment of CD19+ lymphomas and leukemias.