ASX Release

7 May 2026

AROVELLA PRESENTS AT INTERNATIONAL SOCIETY FOR CELL & GENE THERAPY IN DUBLIN TODAY

Highlights:

- **Arovella presents its recent pre-clinical data at the ISCT 2026 Annual Meeting**
- **Data shows Arovella's CLDN18.2-directed CAR-iNKT cells effectively kill CLDN18.2-positive pancreatic cancer and gastric cancer cells in-vitro**
- **CLDN18.2 is a validated therapeutic target in gastric, gastroesophageal junction (GEJ), and pancreatic cancers**
- **Armouring the CLDN18.2 CAR-iNKT cells by incorporating Arovella's IL-12-TM cytokine armouring technology further enhances efficacy**

Arovella Therapeutics Ltd (ASX: ALA), a company focused on developing its invariant Natural Killer T (iNKT) cell therapy platform to treat blood and solid cancers, 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 International Society for Cell and Gene Therapy ISCT 2026 Scientific Annual Meeting in Dublin. The ISCT 2026 is the world's largest cell and gene therapy (CGT) translation conference, bringing together scientific innovators, clinicians, industry leaders, lab professionals, and regulators to advance translational impact across the CGT sector.

The poster, titled *Allogeneic CAR-iNKT cell therapy targeting CLDN18.2-positive gastric and pancreatic cancers,* describes in greater detail the data released in Arovella's announcement on 1 April 2026, CLDN18.2 CAR iNKT Cell Preclinical Data Update. Excitingly, the lead author on the poster, Arovella scientist Dr Clinton Heinze, was also invited to present the poster as an Elevator Pitch oral presentation.

Arovella's Acting Chief Executive Officer, Dr Nicole Van Der Weerden, commented: "We are delighted to have presented our CLDN18.2-CAR-iNKT cell data at ISCT 2026. The data highlights our progress toward developing a CAR-iNKT cell therapy product for solid tumours such as gastric and pancreatic cancer, which is based on our novel CAR-iNKT cell platform. The data demonstrate that CLDN18.2-targeting CAR-iNKT cells potently eliminate CLDN18.2-positive gastric and pancreatic tumour cells. This cytotoxic activity is further enhanced by incorporating Arovella's cytokine armouring technology, IL-12-TM, which is designed to improve cell persistence and long-term anti-tumour activity. This complements the work we are doing with our lead candidate, ALA-101, an allogeneic "off-the-shelf" cell therapy for the treatment of CD19+ lymphomas and leukaemias, which is due to commence phase 1 clinical testing in Q3 2026."

A recent video 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 David Williams, Chairman of the Board of Directors.

FURTHER INFORMATION

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NOTES TO EDITORS:

About Arovella Therapeutics Ltd

Arovella Therapeutics Ltd (ASX: ALA) is focused on developing its invariant natural killer T (iNKT) cell therapy platform based on intellectual property licensed from Imperial College London to treat blood cancers and solid tumours. Arovella's lead product is ALA-101. ALA-101 consists of CAR-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. iNKT cells also express NKG2D, providing a third tumour-recognition mechanism via NKG2D ligands that are upregulated on cancer cells. ALA-101 has secured Investigational New Drug (IND) acceptance from the US FDA and is progressing to a phase 1 clinical trial as an allogeneic cell therapy for the treatment of CD19+ lymphomas and leukaemias, meaning it can be given from a healthy donor to a patient. Arovella's solid-tumour candidate, ALA-105, is a cytokine-armoured CLDN18.2-directed CAR-iNKT cell product developed using CLDN18.2-targeting technology licensed from Sparx Group and incorporating Arovella's IL-12-TM cytokine-armouring technology.

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.

CLDN18.2 – Claudin 18.2, a tight-junction protein normally restricted to gastric mucosal epithelium that becomes accessible on the cell surface of gastric and pancreatic cancers.

IL-12-TM – a membrane-tethered form of Interleukin-12 used as cytokine-armouring technology to enhance CAR-iNKT activity while limiting systemic toxicity.

NKG2D – an activating receptor expressed by NK and iNKT cells that binds stress ligands upregulated on tumour cells.

scFv – single-chain variable fragment, the antigen-binding domain used in a CAR to recognise the tumour antigen target.

For more information, visit www.arovella.com

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

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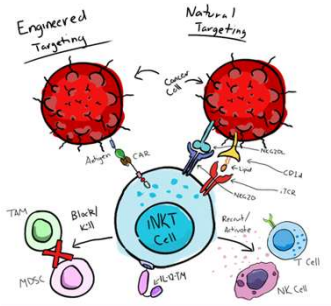
Arovella THERAPEUTICS

#1169

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

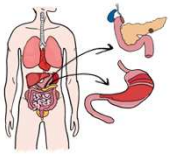
CLDN18.2 is a tight junction protein that is **not present in most healthy tissues**

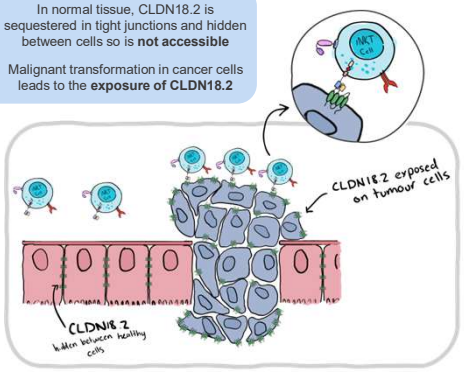
Expression is tightly restricted to gastric mucosal membrane epithelial cells (lining of GI tract)

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

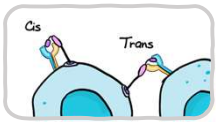
Malignant transformation in cancer cells leads to the **exposure of CLDN18.2**

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)

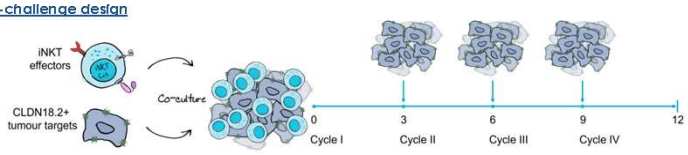


Tethering IL-12 to iNKT cells reduces the toxicity potential relative to exogenous co-administration or secretion of untethered IL-12

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

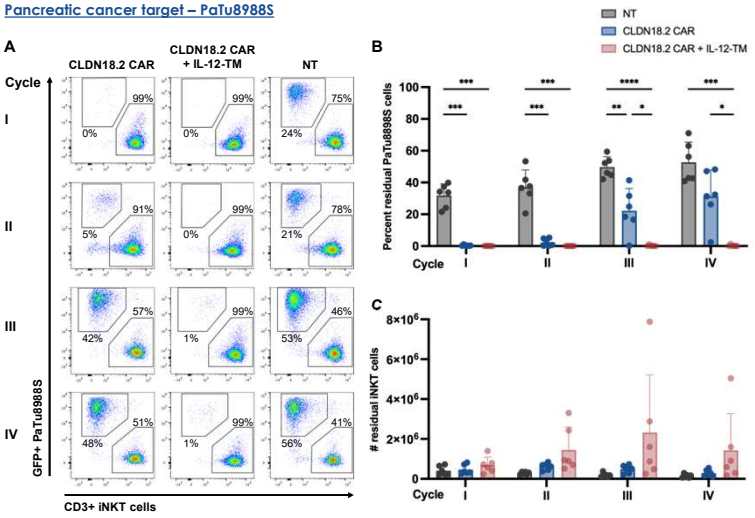
Re-challenge design



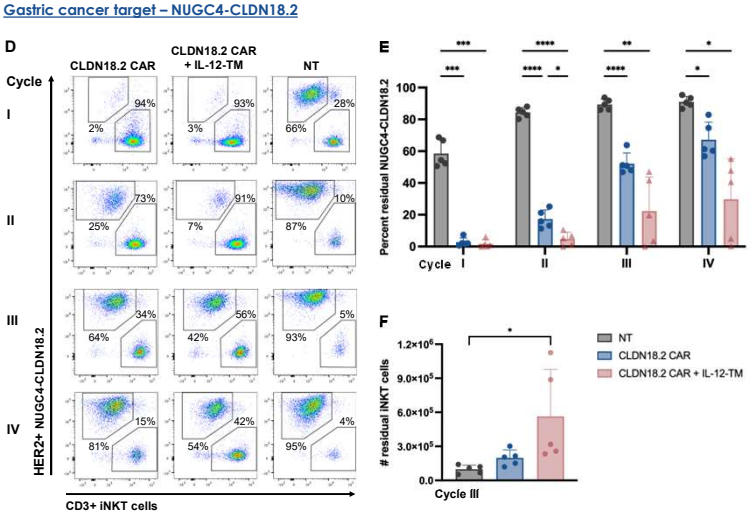
Left: *iNKT cells were co-cultured at a 1:1 CAR+ E:T ratio (PaTu8988S) or 1:2 CAR+ E:T ratio (NUGC4-CLDN18.2) with CLDN18.2+ tumour targets in four parallel wells. At the end of each three-day cycle, one well is harvested, and effector cells in remaining wells were re-seeded with new target cells. Wells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

Below: ***(A)*** *Representative flow plots of six 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 five donors; Summary of the quantification of* ***(E)*** *residual HER2+ NUGC4-CLDN18.2 tumour cells and* ***(F)*** *CD3+ iNKT cells after Cycle III (peak iNKT cell number) 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, **** p<0.0001. 2-way ANOVA with Tukey multi-comparisons and a Geisser-Greenhouse correction. Mean with SD is shown.*

Pancreatic cancer target – PaTu8988S

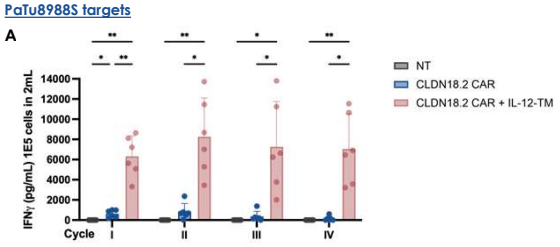


Gastric cancer target – NUGC4-CLDN18.2

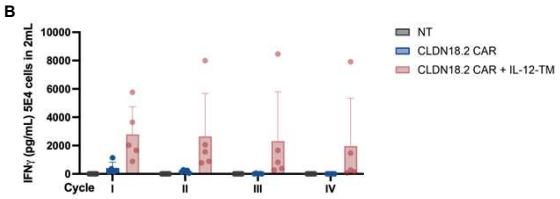


IL-12-TM enhances IFNγ secretion by CAR-iNKT cells in the presence of tumour targets

PaTu8988S targets

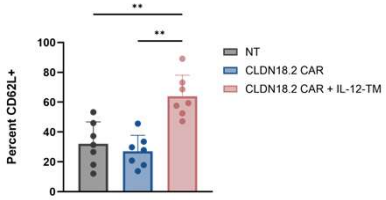


NUGC4-CLDN18.2 targets



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, ** p<0.005. 2-way ANOVA with Tukey multi-comparisons and a Geisser-Greenhouse correction. Mean with SD is shown.*

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



*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).*

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**

Citations

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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-positive 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-positive gastric and pancreatic cancers.
- Arovella's lead candidate, ALA-101, an allogeneic CD19-directed CAR-iNKT cell product has secured IND acceptance and is advancing to a Phase I clinical trial for the treatment of CD19-positive lymphomas and leukemias.