**ASX Release**

10 November 2023

## Chairman's Address to AGM

Following an extensive due diligence period, I joined the board of Arovella therapeutics as Non-executive Chairman in March 2023. Since that time, the Company has continued to make significant progress developing its invariant Natural Killer T (iNKT) cell platform and expanded the potential reach of the technology from blood cancers to solid tumours.

I was delighted to have joined a board with such a deep level of drug development experience, covering academic research, clinical planning and commercial transactions. It is a dynamic board, and importantly spans both hemispheres, which is an important factor as an Australian biotechnology company with its sights set on becoming a global player.

For our lead program, ALA-101, which is being developed for CD19+ heamatological malignancies, or blood cancers we have made excellent progress in 2023. In April, the Company presented its latest developments at the American Association for Cancer Research (AACR) annual meeting in Orlando, in the US. The data was well received, and it highlighted the significant progress the Company made bringing ALA-101 towards clinical trials.

In addition, the group made significant progress on the manufacturing front, a key step for all cell therapy products. The GMP-grade lentivirus is currently on track to be manufactured before the end of the calendar year, and we recently announced our collaboration with Cell Therapies, based in the Peter McCallum Cancer Centre, in Parkville, Melbourne, to manufacture the material for clinical trials. We continue to lay the groundwork to advance ALA-101 into first in human clinical trials in 2024, targeting non-Hodgkin's lymphoma initially.

In addition, the management team scoured the globe for novel technologies that complement Arovella's iNKT cell therapy platform. To that end, the company continued its discussions with University of North Carolina, for an "armouring" technology that will strengthen its iNKT cell platform. In October 2023, we were delighted to enter into an agreement with Sparx Group for their Claudin 18.2 targeting technology, opening up opportunities for solid tumours such as gastric cancer and pancreatic cancer. We have already commenced scientific work to construct a novel Claudin 18.2 targeting iNKT cell, with 2024 shaping up as a year where solid development in this program is anticipated.

We particularly like this target as Astellas Pharma, a US$22 billion Japanese pharmaceutical company, is awaiting US Food and Drug Administration approval for their Claudin 18.2 targeting antibody called zolbetuximab in early 2024 for gastric cancers. This drug has been forecast by Astellas to generate up to US$1.3 billion in peak sales. An approval is expected to increase pharmaceutical company interest in this validated target. Importantly, Arovella's Claudin 18.2-iNKT cells will be the only off-the-shelf

CAR-iNKT cell therapy being developed for this target and will significantly increase the value of Arovella's pipeline.

As a result of some of these activities, Arovella was fortunate the buck the trend of the small cap sector. We are pleased that the Company's share price has increased from the beginning of the calendar year by over 330% to close yesterday at $0.10. This is a remarkable effort in what has been a difficult year for the biotechnology sector, domestically and globally both in terms of absolute share price performance, but also access to capital to continue R&D development.

We are very excited for the year ahead. Thus far, 2023 has been a transformative year for Arovella in terms of team building, strategic acquisitions and it was the year that Arovella formally made the transition to a dedicated cell therapy company. We remain optimistic about our iNKT cell platform and believe that it has the potential to impact patients globally. With that, we would like to thank all our shareholders for their continued support, and who recently supported the Company's efforts in an oversubscribed Placement and Share Purchase Plan in the middle of the year to raise $6.3 million. We look forward to continuing to build shareholder value in the years to come.

Dr Tom Duthy

Chairman

ASX:**ALA**

arovella
THERAPEUTICS

# Annual General Meeting

## November

2023

# Arovella's Board of Directors

## Dr. Tom Duthy

CHAIRMAN

Dr Duthy has over 18 years of direct financial markets experience and is the Founder and CEO of Nemean Group Pty Ltd, a boutique corporate advisory and investor relations firm specialising in the life sciences and technology sectors. Tom spent ten years as a leading sell-side Healthcare & Biotechnology analyst at Taylor Collison Limited, focused mainly on small caps.

Neurotech · SIRTeX · invex THERAPEUTICS · NEMEAN

## Dr. Michael Baker

CEO & MANAGING DIRECTOR

Over 15 years experience in scientific research, drug development and venture investing sectors. He was an Investment Manager with the leading Australian life science fund, BioScience Managers. He also conducted due diligence to shortlist investment opportunities and played an active role in managing portfolio companies.

BioScience Managers · The University of Melbourne · Melbourne Business School · hexima

## Dr. Debora Barton

DIRECTOR

Dr. Barton has over 20 years of oncology experience, in academia, as a practicing physician and in the biotechnology / pharmaceutical industry. She served in key senior executive positions, including Carisma Therapeutics and TScan Therapeutics, where Dr. Barton is currently the Chief Medical Officer, and Advanced Accelerator Applications, acquired by Novartis during Debora's tenure.

Celgene · NOVARTIS · TSCAN THERAPEUTICS

## Mr. David Simmonds

DIRECTOR

David was a senior audit partner with Ernst & Young from 1989 to 2017. From 2008 to 2013, David led the Capital Markets desk in Australia with responsibility for overseeing or reviewing all Australian cross border fundraisings. David was a member of the Board of MS Research Australia.

MS Research Australia · EY Building a better working world

## Dr. Liz Stoner

DIRECTOR

Dr. Stoner is a distinguished biopharma executive, who brings decades of international industry experience to her role, including senior roles in Clinical Development Operations at Merck Research Laboratories. Liz is an Executive Partner at MPM Capital, and she has held numerous leadership roles at MPM portfolio companies. Liz was previously an Assistant Professor of Pediatrics at Cornell University Medical College.

MPM Powering Breakthroughs in Life Sciences · Cornell University Founded A.D. 1865 · MERCK

## Mr. Gary Phillips

DIRECTOR

Mr. Phillips has more than 30 years of operational management experience in the pharmaceutical and healthcare industry in Europe, Asia and Australia. He is currently the CEO and Managing Director of the ASX-listed company, Pharmaxis – previously he was the CEO at Ciba Geigy in Hungary (Merged to form Novartis in 1996) where he led the successful launch of a portfolio of new products.

NOVARTIS · pharmaxis

# CEO & MD address

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# Key achievements for FY23

FY2023 was a transformative year for Arovella and its proprietary iNKT cell platform

## Completed the transition to be solely focused on iNKT cell therapies

- Strengthened the Board and Management Team to deliver on objectives
- Closed Perth R&D facility to reduce overheads
- Raised ~$8 million to fund development of ALA-101 and the iNKT cell platform

## Completed key manufacturing activities for ALA-101 in preparation for phase 1 clinical trials

- Finalised lentiviral vector design for ALA-101 and demonstrated potent anti-tumour activity *in vitro* and *in vivo*
  - data presented at AACR in April
- Commenced GMP manufacturing of lentiviral vector with Lentigen
- Commenced scale-up of ALA-101 manufacturing process at Cell Therapies Pty Ltd

## Continued to enhance the iNKT cell platform

- In-licensed a novel target for solid tumours (Claudin 18.2)
- Optioned a cytokine technology which enhances the persistence and activity of CAR-iNKT cells
- Progressed research collaboration with Imugene after positive *in vitro* data demonstrating ALA-101 works in combination with onCARlytics

# Financial overview

## Financial Snapshot

| ASX CODE | ALA |
|---|---|
| Market capitalisation[1] | $81.5 million |
| Shares on issue | 906.31 million |
| 52-week low / high[1] | $0.020 / $0.105 |
| Cash Balance (September 30 2023)[2] | $5.32 million |

## Major Shareholders

| Shareholder | Ownership (%) [1] |
|---|---|
| THE TRUST COMPANY (AUSTRALIA) LIMITED | 59,397,161 (6.66%) |
| RICHARD JOHN MANN | 50,905,657 (5.71%) |
| UBS NOMINEES PTY LTD | 20,620,196 (2.31%) |
| BLACKBURNE CAPITAL PTY LTD | 18,325,000 (2.05%) |
| DYLIDE PTY LTD | 15,666,666 (1.76%) |

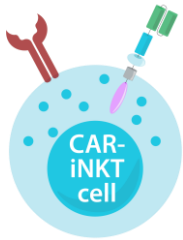

1. *As of 8 November 2023*
2. *Does not include the R&D tax incentive rebate of approximately $2m expected in Q4 2023*

# Recent cell therapy transactions[1]

| Date | Type of deal | Acquirer/Licensee | Target/Licensor | Cell Type | Stage | Upfront (US$M) | Milestones (US$M) | Total deal value (US$M) |
|---|---|---|---|---|---|---|---|---|
| Nov-23 | Collaboration and investment | AstraZeneca | cellectis | Not specified | Platform | $25 | $70-220 per product | |
| Aug-23 | Licence[2] | IMUGENE Developing Cancer Immunotherapies | PRECISION BIOSCIENCES | T Cell | Phase 1b | $21 | $206 | $227 |
| Aug-23 | Strategic investment (ROFR) [3] | astellas | POSEIDA THERAPEUTICS | T Cell | Phase 1 | $25 | $0 | $25 |
| May-23 | Licence | janssen | CBMG Cellular Biomedicine Group | T Cell | Phase 1b | $245 | *undisclosed* | |
| Jan-23 | Acquisition | AstraZeneca | neogene THERAPEUTICS | T Cell | Phase 1 | $200 | $120 | $320 |
| Oct-22 | Development collaboration[4] | GILEAD | ARCELLX | T Cell | Phase 2 | $225 | *undisclosed* | |
| Sep-22 | Research collaboration | Genentech A Member of the Roche Group | ArsenalBio | T Cell | Preclinical | $70 | *undisclosed* | |
| Aug-22 | Licence & strategic collaboration | Roche | POSEIDA THERAPEUTICS | T Cell | Phase 1 | $110 | $110 | $220 |
| Sep-21 | Development collaboration | Genentech A Member of the Roche Group | Adaptimmune | T Cell | Preclinical | $150 | $150 | $300 |
| Aug-21 | Research collaboration | GILEAD | APPIA BIO | iNKT Cell | Preclinical | *undisclosed* | *undisclosed* | $875 |
| May-21 | Acquisition | Athenex | kuur THERAPEUTICS | iNKT Cell | Phase 1 | $70 | $115 | $185 |
| Jun-21 | Acquisition | eterna | Novellus THERAPEUTICS | Multiple | Preclinical | $125 | $0 | $125 |
| Dec-19 | Acquisition | astellas | XYPHOS | Multiple | Preclinical | $120 | $545 | $665 |

1. *See Slide 21 for deal references*
2. *Cellectis will receive a US$220m equity investment from Astra Zeneca plus tiered royalties. Milestones are payable for 10 products*
3. *Precision is eligible for double digit royalties on net sales and $145 million in milestone payments and tiered royalties for additional programs*
4. *Poseida also received a US$25m equity investment from Astellas*
5. *Arcellx also received a US$100m equity investment from Gilead*

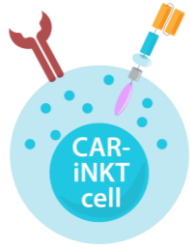
# Arovella's expanding pipeline




CD19-CAR


CD19-CAR

Oncolytic virus
CF33-CD19




**Novel Targets**

**Introduction of CLDN18.2**

**ALA-101**

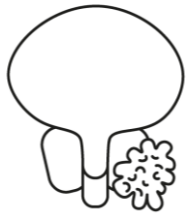
**ALA-101 + onCARlytics**

**CLDN18.2 and DKK1**

**Cytokine Technology**

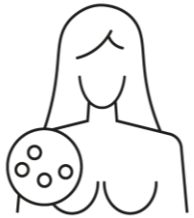
Non-Hodgkin's Lymphoma

Head and Neck Cancer



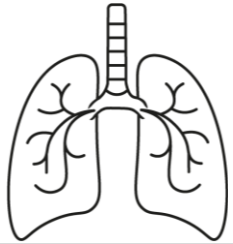
Prostate Cancer

Brain Metastases

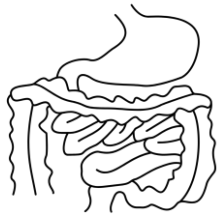


Triple negative breast cancer

Pancreatic Cancer



Lung Cancer



Gastric Cancers

# Progress towards first-in-human clinical trials

## ALA-101 data confirms activity and off-the-shelf capability

### Potent Antitumour Activity

Demonstrated efficacy of ALA-101 against CD19+ lymphomas and leukemias. Proof-of-concept data generated with clinical-design lentiviral vector in animal models using thawed, “off-the-shelf” ALA-101.

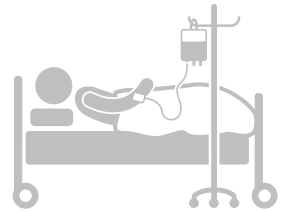
### Expected to be Safe

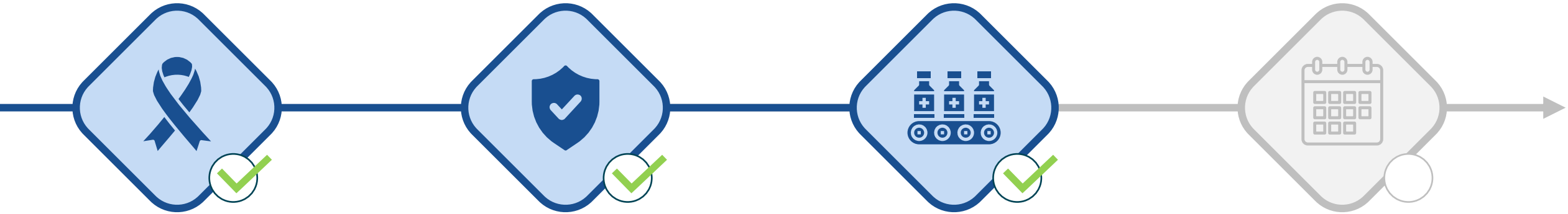
iNKT cells have been shown in clinical trials not to cause graft versus host disease (GvHD) and the CD19 targeting CAR (FMC63) is a validated targeting agent in approved cell therapies.

### Multiple Dose Manufacturing

ALA has demonstrated that its manufacturing process can produce a high number of CAR+ cells with potent cell killing properties and has commenced production of GMP-grade lentivirus for CD19 CAR expression.

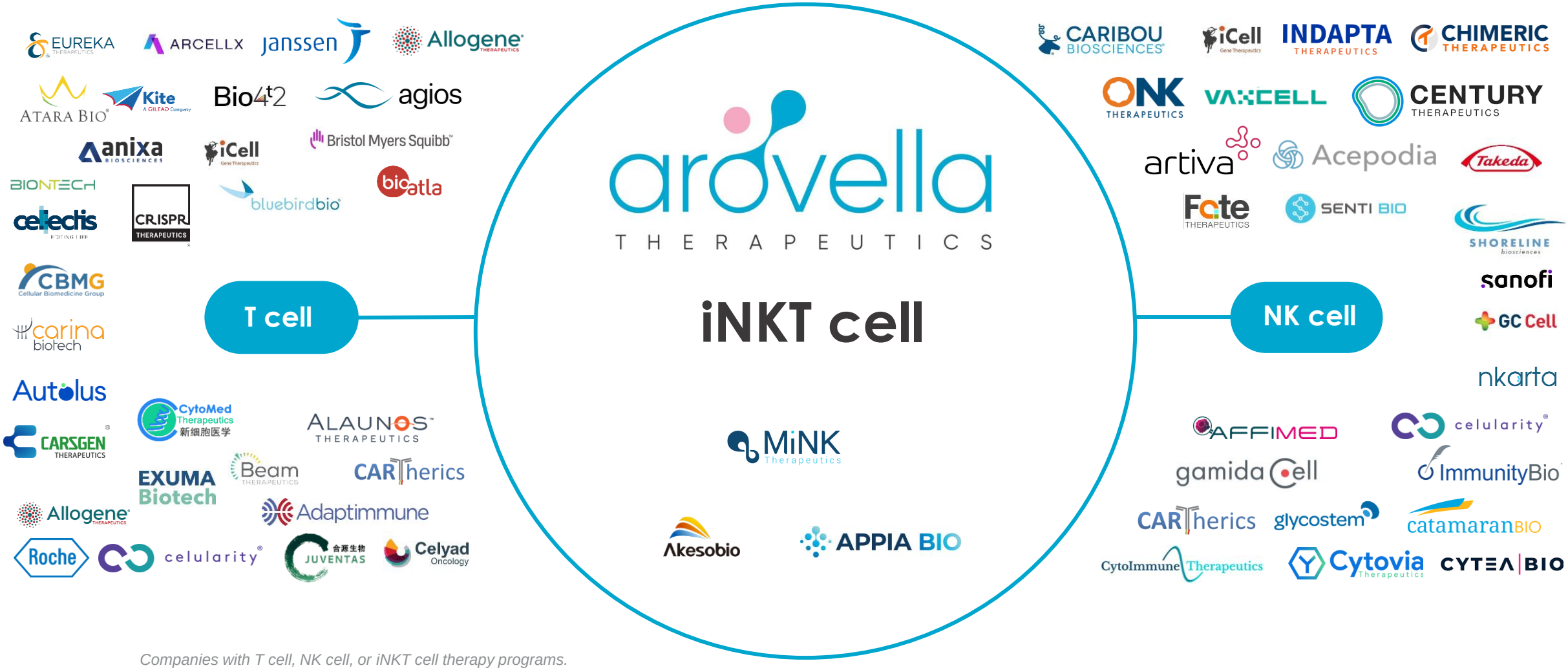
### Phase 1 Clinical Trial





# A differentiated position

## T cell and NK cell sectors are competitive




*Companies with T cell, NK cell, or iNKT cell therapy programs.*
*Source: Company analysis based on public information*

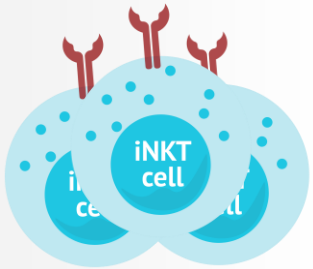
# CAR-iNKT cell therapy production advantages

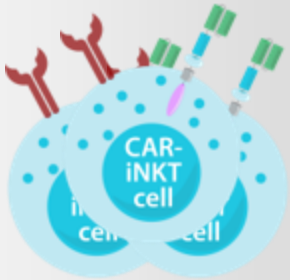
## Off-the-shelf manufacturing advantages

MANUFACTURING

Collect Healthy Donor Blood

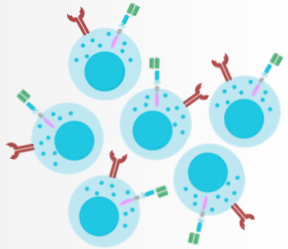
Isolate iNKT cells




Engineer iNKT cells to produce a CAR

Expand to grow billions of CAR-iNKT cells

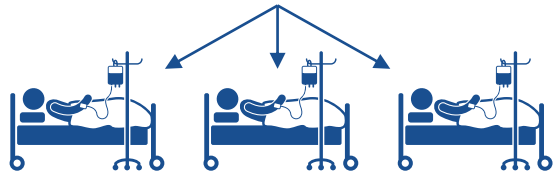


Vial and freeze CAR-iNKT cells

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 to target solid tumours

Arovella is implementing its strategy to target and kill solid tumours – 90% of newly diagnosed cancer cases[1]

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

# 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 iNKT cells with novel armouring technologies

## Create unique partnerships

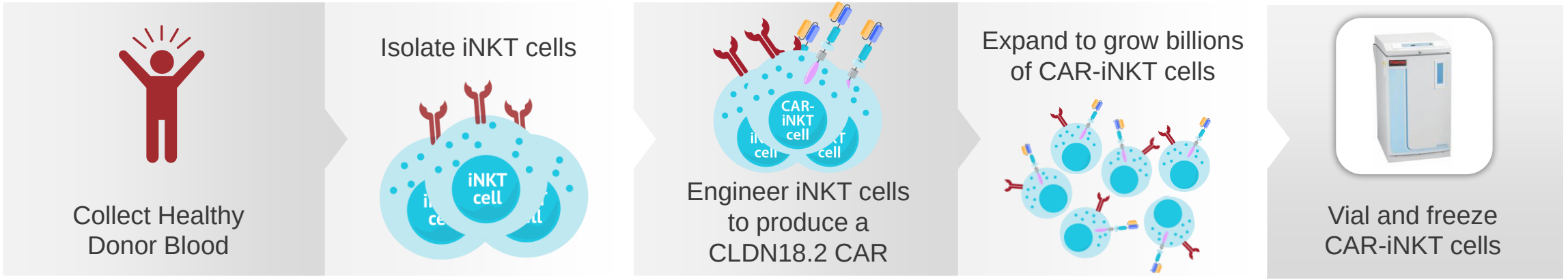
Create partnerships to use novel combination therapies with synergistic effects

# Manufacturing CLDN18.2-iNKT cells

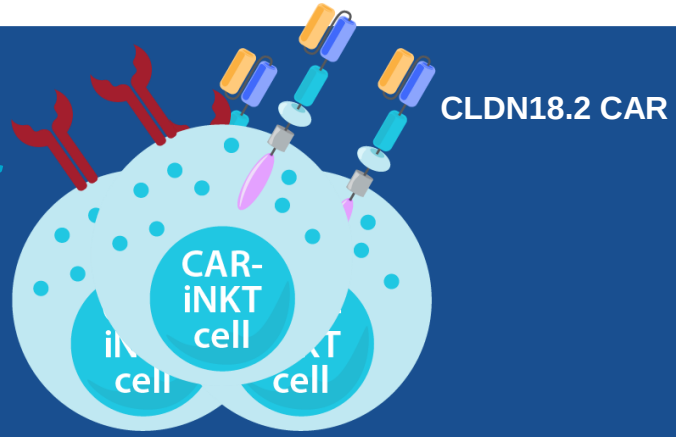
STRATEGY 1

## Generation of CLDN18.2-iNKT cells will leverage existing manufacturing process

MANUFACTURING




Arovella will use its **proprietary manufacturing process** to create CLDN18.2-iNKT cells



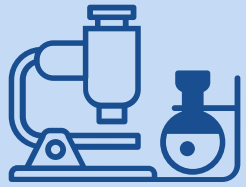
# Introducing Claudin 18.2 (CLDN18.2)

## A promising solid tumour target

CLDN18.2 overexpression has been

**identified in several types of cancers**

- gastric cancer **(GC)**
- gastroesophageal junction cancer **(GEJC)**
- pancreatic cancer **(PC)**
- esophageal cancer **(EC)**
- ovarian adenocarcinoma **(OAC)**
- lung cancers **(LC)**



**Validated target**

with first monoclonal antibody expected to be **approved in 2024**

**Gastric cancer**

market alone expected to reach **$10.7 billion** by 2031[1]

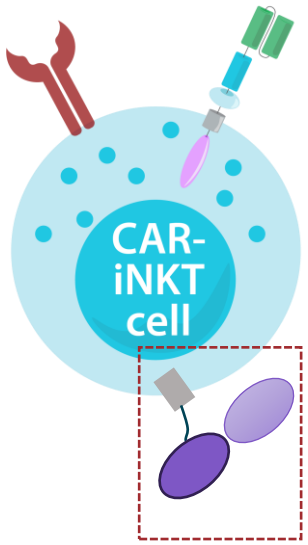
*1. https://www.alliedmarketresearch.com/gastric-cancer-market-A74458#:~:text=The%20global%20gastric%20cancer%20market,cells%20lining%20of%20the%20stomach*

# “Armouring” iNKT cells

STRATEGY 2

## Cytokine technology enhances activity of iNKT cells in solid tumours

## Cytokine Technology




Cytokine Technology

Adding specialised cytokines to iNKT cells can **increase persistence of the cells** *(how long they last in the body)* and increase anti-tumour activity

**Exclusive option**

with University of North Carolina for cytokine technology developed by Prof. Gianpietro Dotti

Cytokine technology is incorporated into the lentiviral vector and **does not require change to manufacturing process**

## iNKT cells + cytokine technology

**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

**75%+**
of mice treated with CAR-iNKT cells containing the cytokine were **alive at 61 days**

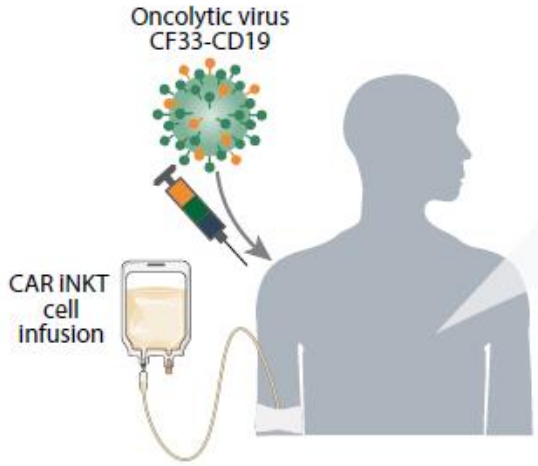
VS

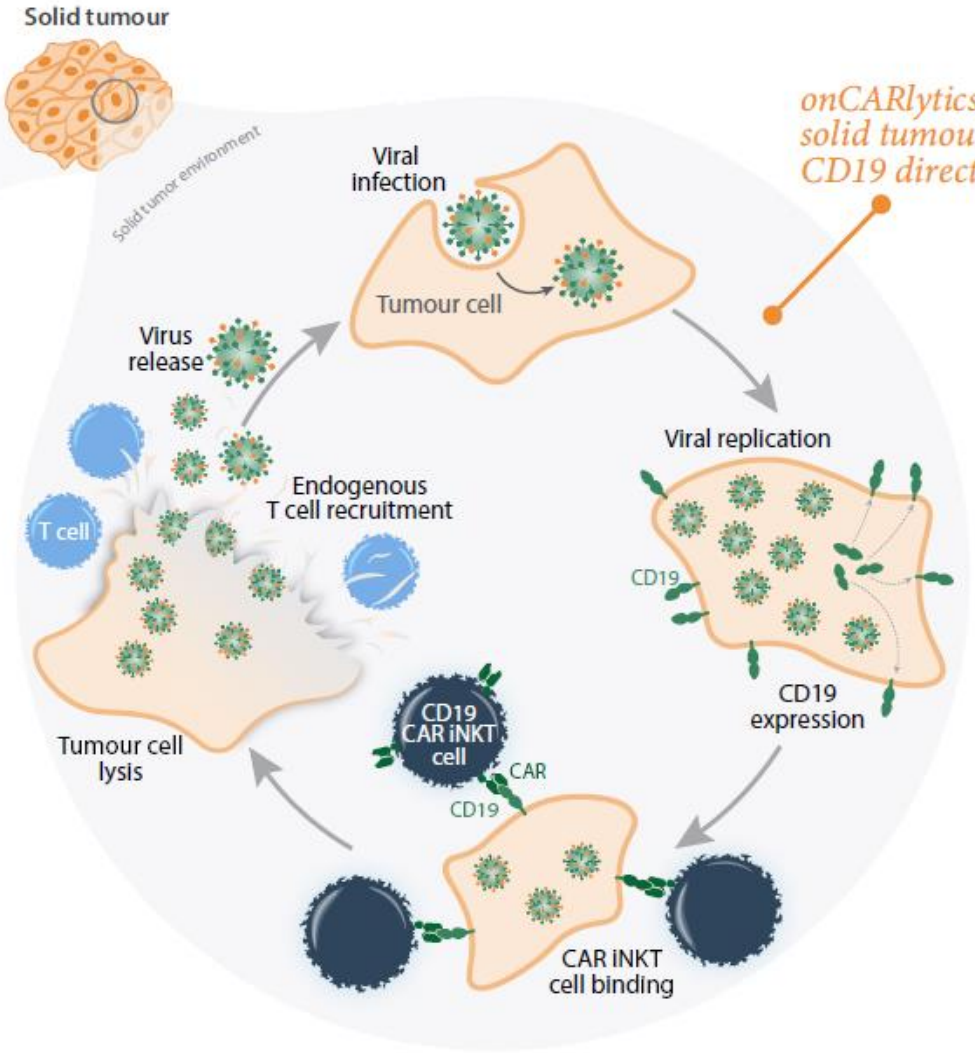
**0%**
of mice treated with CAR-iNKT cells lacking the cytokine **were alive at 49 days**

# ALA-101 & Imugene's onCARlytics

STRATEGY 3

## Imugene's onCARlytics platform may make solid tumours sensitive to ALA-101




*onCARlytics makes solid tumours "seen" by CD19 directed therapies*

1. OnCARlytics infects tumour cells
2. Virus replication and production of CF33-CD19 on the cell surface enabling CD19 targeting
3. Tumour cell lysis leads to viral particle release and the combination promotes endogenous immune cell recruitment to tumours
4. Released viral particles re-initiate virus infection of surrounding tumour cells.

**Expecting in vivo data in H2 2023**

# Milestones for FY2024

| | June 2023 | December 2023 | June 2024 |
|---|---|---|---|
| ALA-101 | ▪ Complete process optimisation and scale-up in preparation for cGMP manufacture<br>▪ Complete production of cGMP lentiviral vector<br>▪ Finalise clinical trial plan for Phase 1 study | ▪ Complete cGMP manufacture for Phase 1 clinical trials<br>▪ Complete preparatory activities for Phase 1 study, including submission of regulatory dossier, engagement with clinical sites and KOLs | |
| iNKT Cell Therapy Platform | ▪ Confirm the activity of ALA-101 cells when combined with Imugene's onCARlytics to target solid tumours in animal models<br>▪ In-licence cytokine technology currently under option (pending due diligence) | ▪ Initiate proof-of-concept testing for CLDN18.2-iNKT cells to expand iNKT platform for treatment of solid tumours | |

## 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

## Continue to enhance the platform and expand the pipeline

Expand the use of the iNKT platform to treat solid tumours

*cGMP – Current Good Manufacturing Practice; KOLs – key opinion leaders*

# Summary

## Novel allogeneic CAR-iNKT cell platform

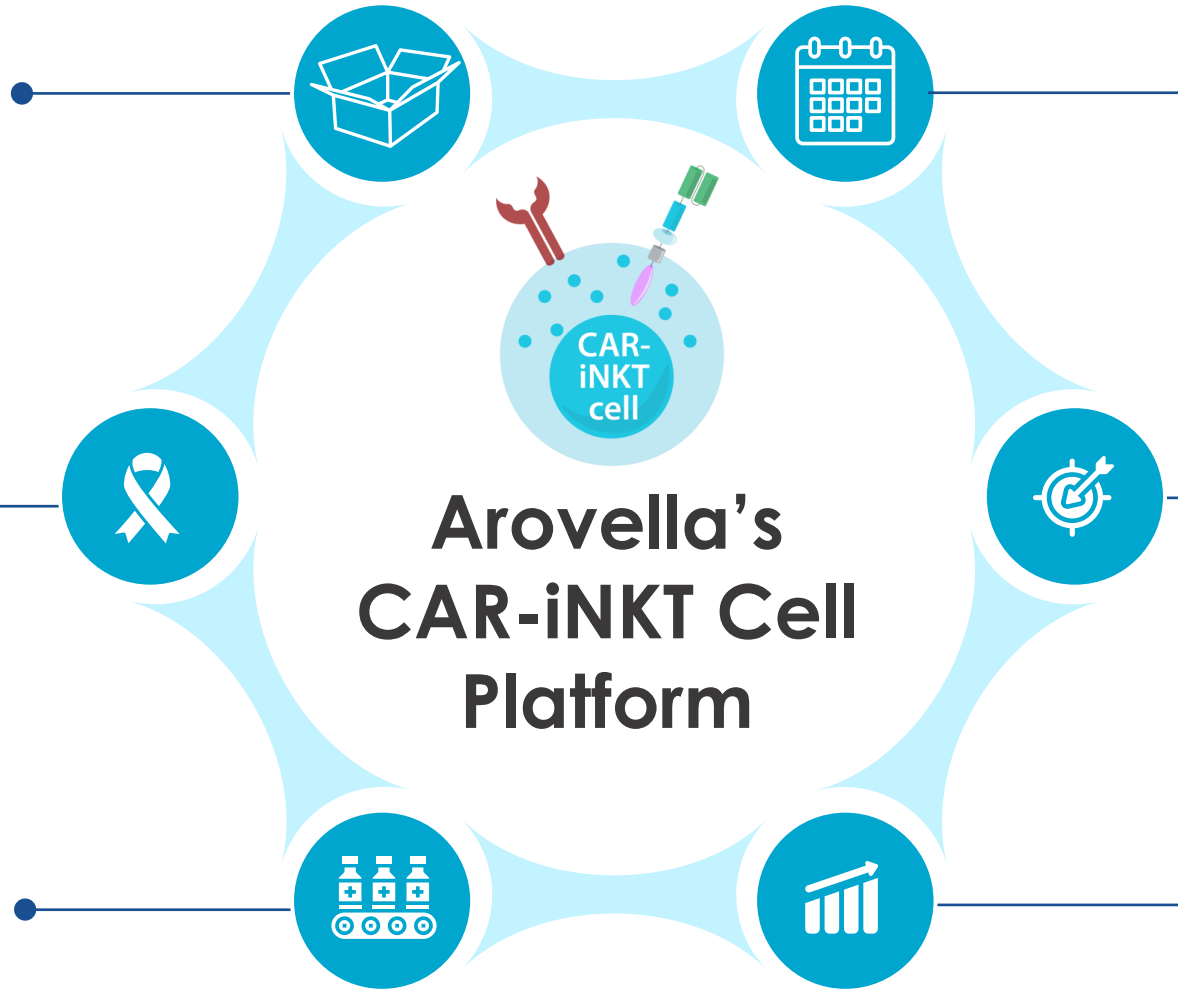
iNKT cells serve as an excellent platform to develop allogeneic, or “off-the-shelf”, cell therapies to treat cancer

## Improved manufacturing logistics

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

## CAR-iNKT cells have multiple anticancer properties

CAR-iNKT cells have multiple anti-cancer properties that may support enhanced efficacy over other immune cell types




## Lead product progressing to clinical trials

ALA-101, a potential treatment for CD19+ blood cancers, is being progressed to Phase 1 clinical trials, expected to commence in 2024

## Arovella has an expanding pipeline

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

## Arovella is poised for growth

Arovella’s CAR-iNKT cell therapy platform is highly differentiated, and the Company has an expanding pipeline and a strong leadership team

ASX:**ALA**

arovella
THERAPEUTICS

# Thank You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