



Rearming the immune system to fight cancer

## Driving Next Generation Cell Therapies with CAR-T/NK Cell Manufacturing

**Ian Nisbet, Chief Operating Officer**

2<sup>nd</sup> Annual Australia Biologics Festival 2024, 22-Feb-2024

### Acknowledgement of Traditional Owners

In the spirit of reconciliation, Cartherics acknowledges the Traditional Custodians of country throughout Australia and their connections to land, sea and community. We pay our respect to their Elders past and present and extend that respect to all Aboriginal and Torres Strait Islander peoples today.



# Cartherics Pty Ltd

*Established to create a powerful allogeneic iPSC-derived cell therapy platform for the treatment of cancer*



## Private company

- Based in Melbourne, Australia
- Commenced operations Jan 2016
- Currently ~30 employees



## Funding

- Raised >AUD\$44M in private investment and grants



## Facilities

- Purpose-built, 18,600 sq ft R&D facility opened 2022
- Clean room capacity for clinical trial production

## Products

### Allogeneic platform

- Primary focus
- iPSC-derived cells
- Feeder-free differentiation
- First product to enter the clinic in 2025

### An autologous CAR-T cell product

- Proof of concept for CAR constructs and gene edits
- Due to enter the clinic in 2024/25 via clinical collaborators

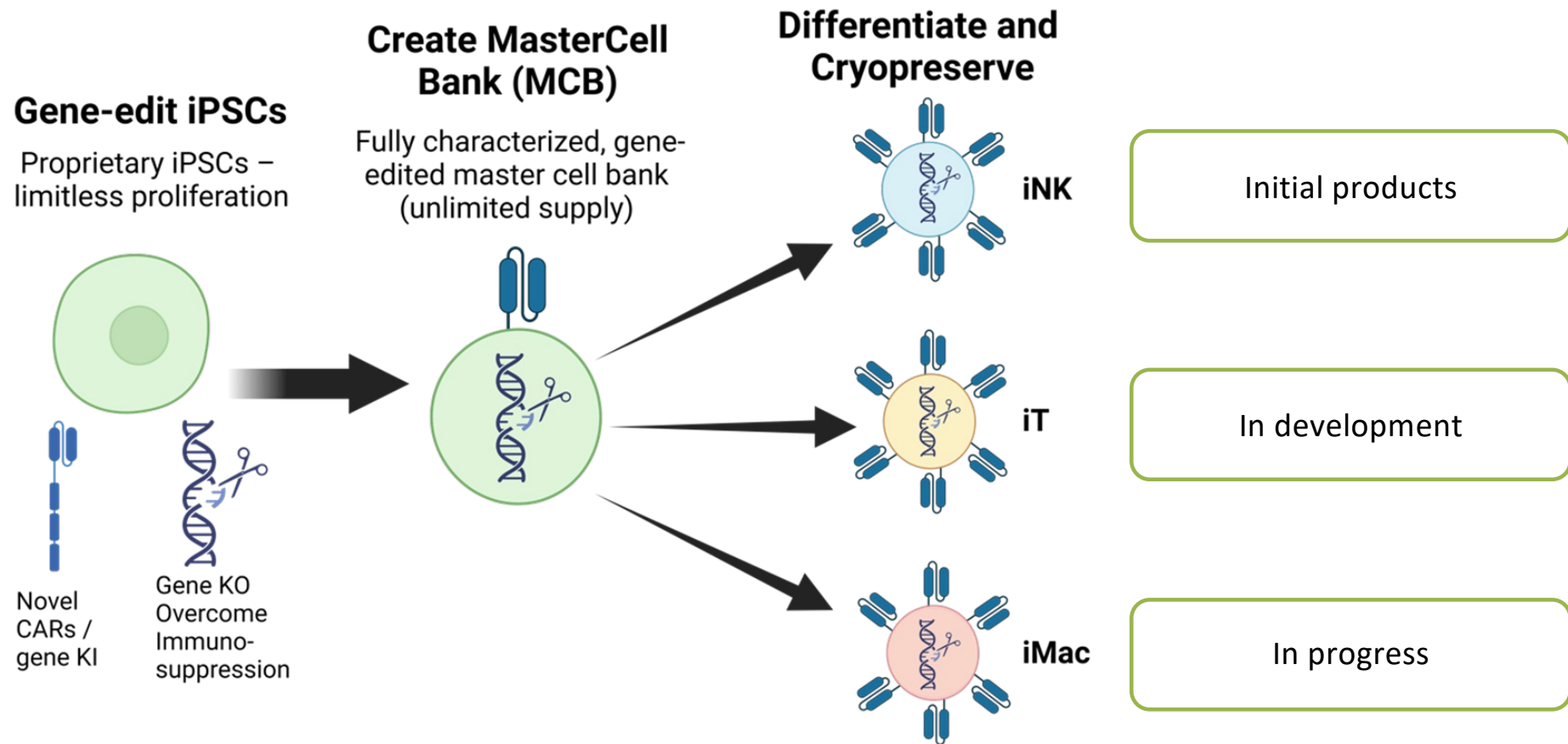
# The Future of Cell Therapies is “Off-the-Shelf”

*Only iPSC-derived allogeneic products will unlock the full potential of immune cell therapies*

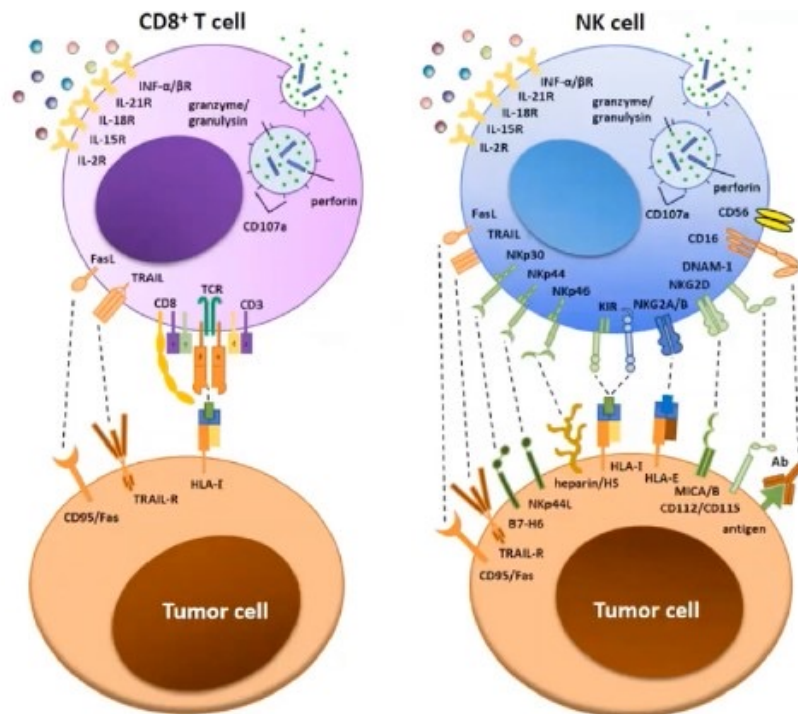
Patient-derived autologous cell therapies		Donor-derived allogeneic cell therapies		iPSC-derived cell therapies	
Cell source	<ul style="list-style-type: none"> <li>Patient-derived, variable quality</li> </ul>	Cell source	<ul style="list-style-type: none"> <li>Cord blood or donor PBMC-derived</li> <li>Donor variation</li> </ul>	Cell source	<ul style="list-style-type: none"> <li>✓ Fully characterised, gene-edited master cell bank (unlimited supply)</li> </ul>
Manufacture	<ul style="list-style-type: none"> <li>Patient variation</li> <li>Extremely high COGS</li> </ul>	Manufacture	<ul style="list-style-type: none"> <li>Ongoing donor supply required</li> </ul>	Manufacture	<ul style="list-style-type: none"> <li>✓ One product treats multiple patients</li> <li>✓ Reduced COGS</li> <li>✓ Batch consistency</li> </ul>
Product Features	<ul style="list-style-type: none"> <li>Random gene insertion</li> <li>Heterogeneous</li> <li>Limited characterisation</li> </ul>	Product Features	<ul style="list-style-type: none"> <li>Heterogenous</li> <li>Inefficient gene-editing for some cell types</li> <li>Limited characterisation</li> </ul>	Product Features	<ul style="list-style-type: none"> <li>✓ Precisely gene-edited</li> <li>✓ Homogenous</li> <li>✓ Fully characterised</li> </ul>
Delivery to patient	<ul style="list-style-type: none"> <li>Time delay between eligibility and treatment</li> </ul>	Delivery to patient	<ul style="list-style-type: none"> <li>On demand</li> </ul>	Delivery to patient	<ul style="list-style-type: none"> <li>✓ On-demand</li> </ul>
Platform potential	<ul style="list-style-type: none"> <li>Limited ability to scale for non-niche indications</li> </ul>	Platform potential	<ul style="list-style-type: none"> <li>Dependent on isolation of different cell types from donors</li> </ul>	Platform potential	<ul style="list-style-type: none"> <li>✓ Applicable to multiple immune cell products</li> </ul>

# Cartherics' Allogeneic Cell Therapy Platform

*Provides ability to rapidly develop multiple products, multiple cell types*



# Initial focus on iNK Cells



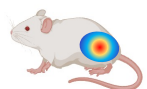
## Advantages of CAR-NK over CAR-T cells

- Multiple mechanisms for tumor cell killing
  - Natural cytotoxicity through NK cell receptors to complement CAR-mediated cell killing and overcome antigen escape
- Better safety profile
  - Anti-tumor effect without GvHD
  - Favorable cytokine profile
  - Low risk of “cytokine storm”
  - Low risk of neurotoxicity



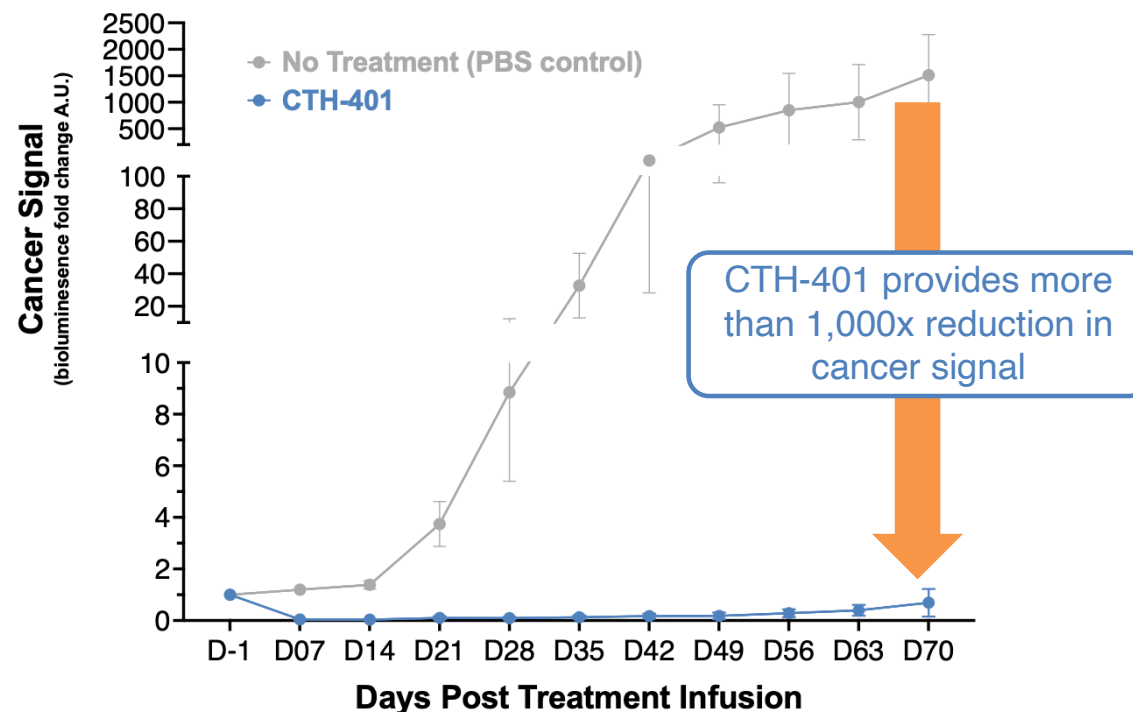
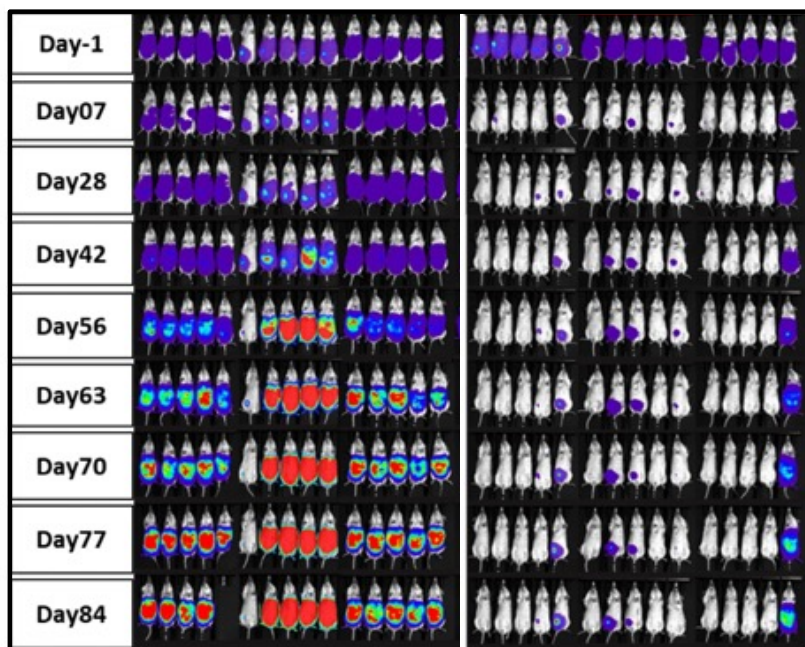
# Our Team Lives for Results Like These

*CTH-401 destroys ovarian cancer in mouse models and shows sustained efficacy*

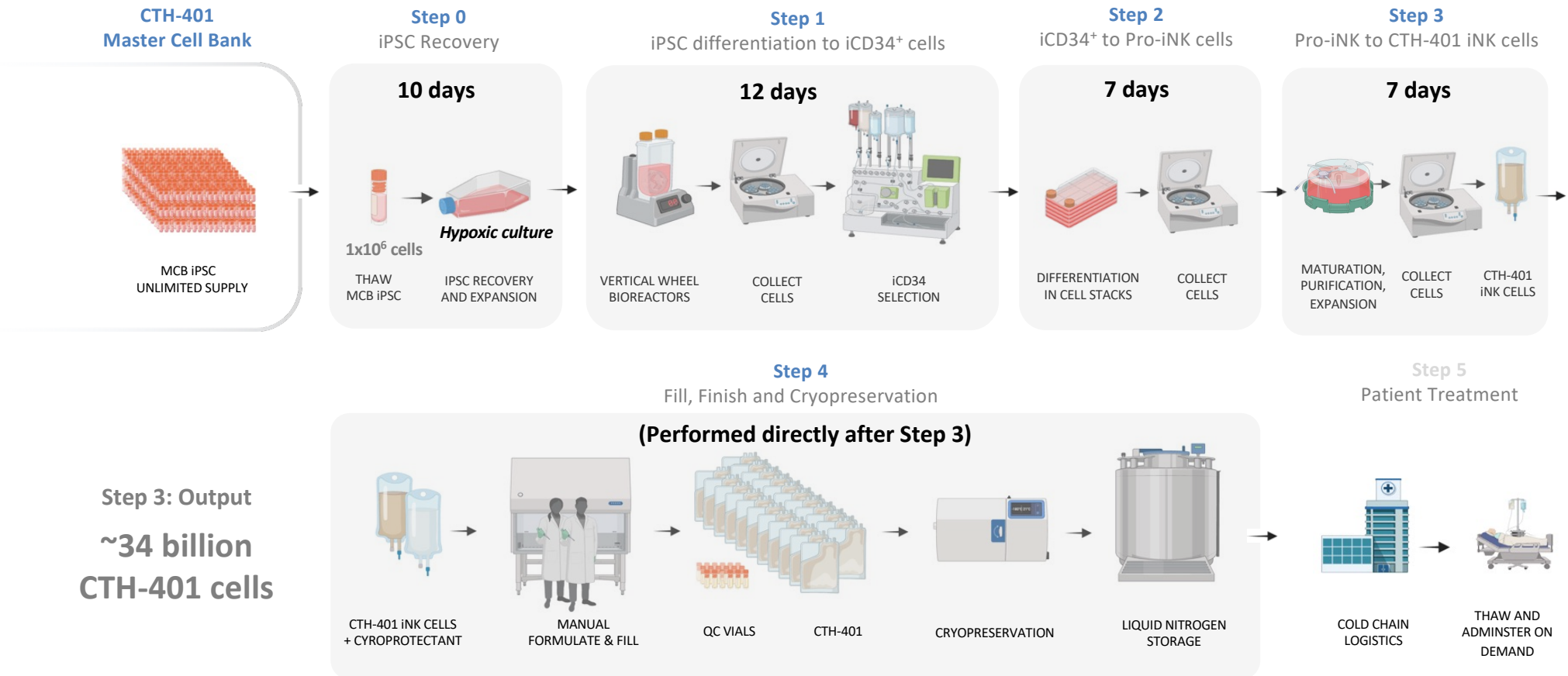


**No Treatment**  
(PBS control)

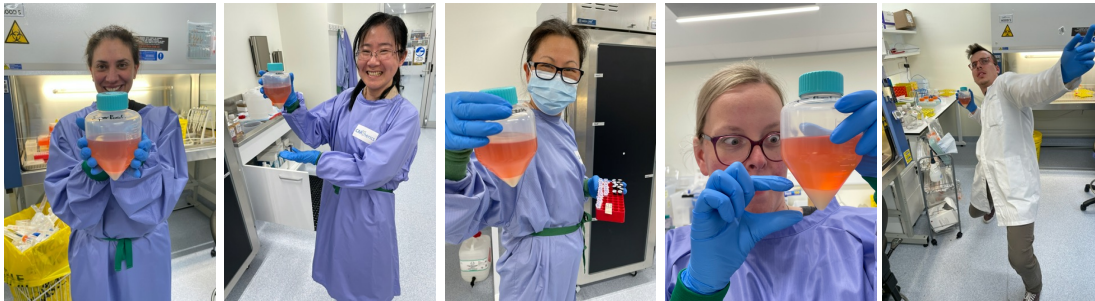
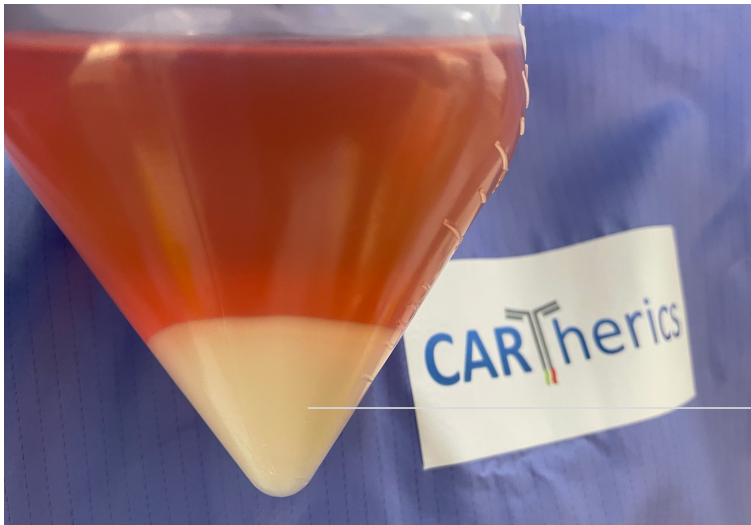
**CTH-401**



# Scalable Method of Manufacture



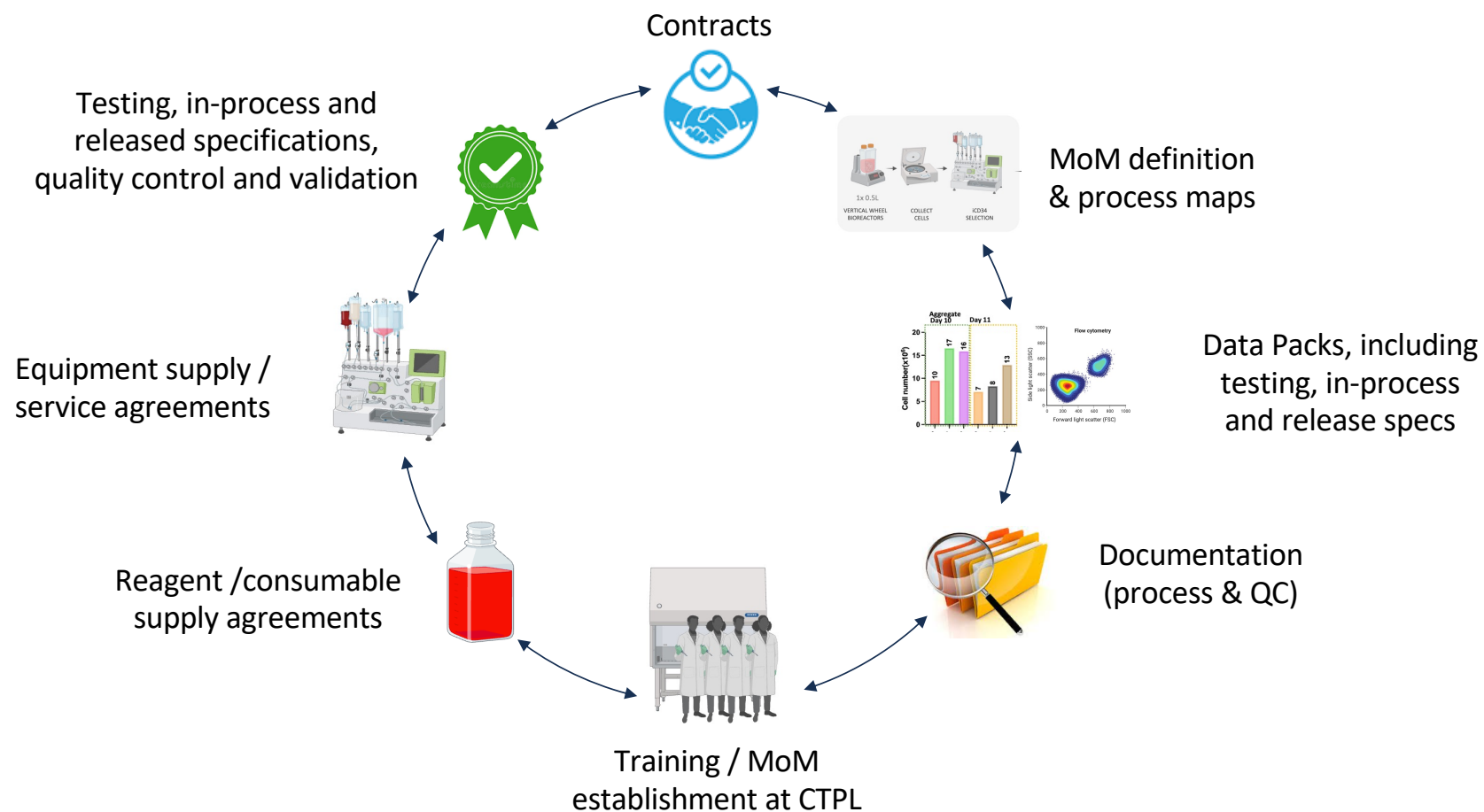
# This is What 20 Billion iNK Cells Looks Like





# Technology Transfer to CMO

*Method of manufacture is currently being transferred to Cell Therapies Pty Ltd*



# Lessons

- Know when to hold-em and know when to fold-em
- Move to bioreactor-based processes and closed systems as soon as possible
- Simplify and standardize (everything – reagents, consumables, terminology)
- Avoid research grade reagents where no GMP version is available
- Define batch release and in-process criteria early
- Establish quality and documentation systems early
- Write-up in real time – if it's not documented, it hasn't been done

# Drug Development is the Ultimate Team Sport

