REVOLUTIONARY CAR-T PLATFORM FROM UNIVERSITY OF PENNSYLVANIA

OUT IN FRONT OF THE BIGGEST WAVE IN ONCOLOGY

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Please see our website for supplemental COVID-19 Risk Factors

Prescient Therapeutics

CAR-T has been a paradigm-changing development in cancer treatment…

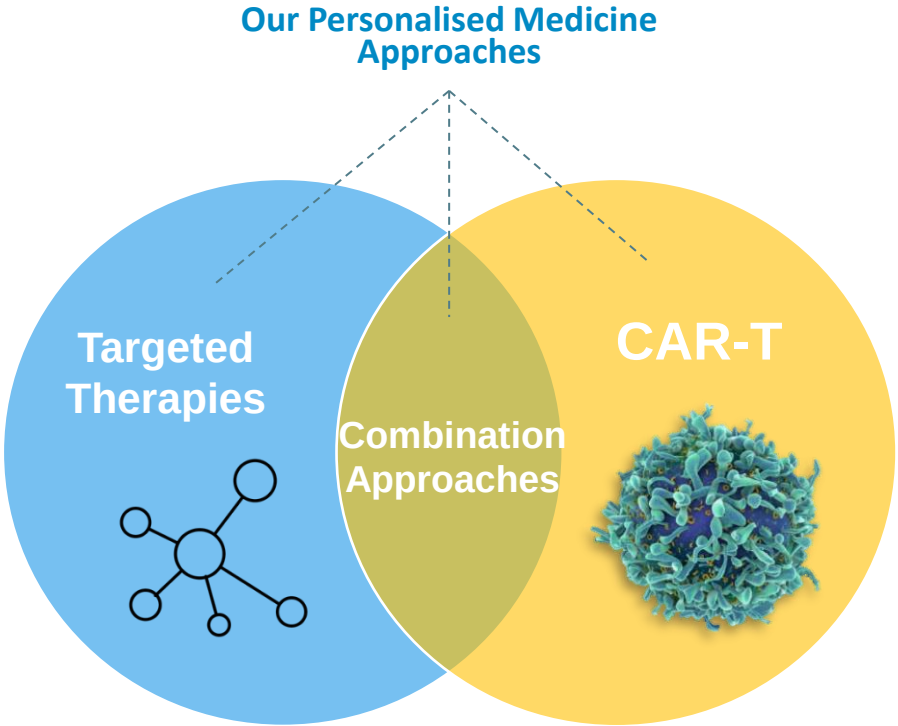
…now we're about to make it a whole lot better.

Presentation **Summary**

- **Transformational technology** from UPenn - the global leader in CAR-T
- Catapults PTX to the **forefront of CAR-T** development
- **Addressing the biggest problems** in the **most exciting area** of oncology
- An **enabling platform** not just for Prescient, but for **any other CAR-T player**
- Many development, collaboration and licensing possibilities!

What We Do

- ASX Listed biotech (ASX: PTX)
- Developing personalised medicines for cancer
  - Targeted therapies
  - CAR-T
- Close relationships with world-leading centres in US and Australia
  - License from the best in field
  - Collaborate with the best in field



Our Goals

- To develop personalised cancer therapies to improve patient outcomes
- Focus on unmet or poorly met clinical needs
- Develop revolutionary technologies to bring the success of CAR-T to more patients
- Dramatically increase efficacy and control of CAR-T technology
- Drive down the cost and time for cancer treatments
- Become a leading, enabling technology for cell therapy approaches

Emily Whitehead, aged 6

Suffering a blood cancer called acute lymphoblastic leukemia.

After 16 months of chemotherapy, and two relapses, her leukemia still persisted.

Doctors told her parents that Emily would not survive.

Emily's parents, searching for a miracle, enrolled her in a trial at UPenn as the very first patient to receive a radical new treatment called…CAR-T.

Emily Whitehead today.

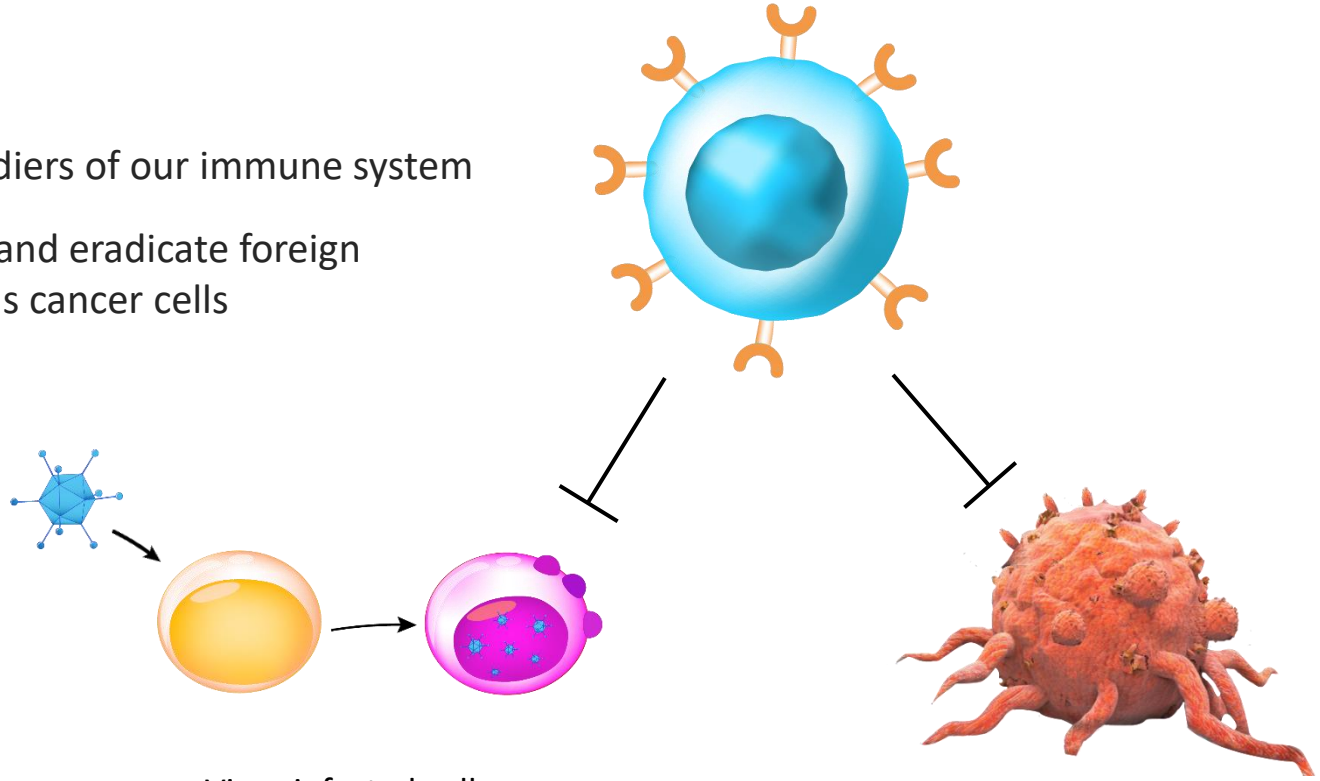
- *"CAR T represents **a turning point in the history of human medicine**, a **genuine revolution in our approach to disease**."*[1]
- Response rates of ~80% in certain lymphomas[2]
- Today CAR-T is riding the crest of a second wave of innovation - the goal is a **universal CAR-T platform** that massively increases its application beyond certain haematological blood cancers with the potential to save millions of people every year.

Emily Whitehead Foundation
Photo taken May 2020

1. CAR-T and The Rise of the Cellicon Valley; UPenn, 2017; https://www.med.upenn.edu/cart/
2. Cleveland Clinic, 2020

Firstly, what are T-cells?

- T-cells are the soldiers of our immune system
- They can identify and eradicate foreign invaders, as well as cancer cells



Virus-infected cells

Cancer cells

How do they work?

1

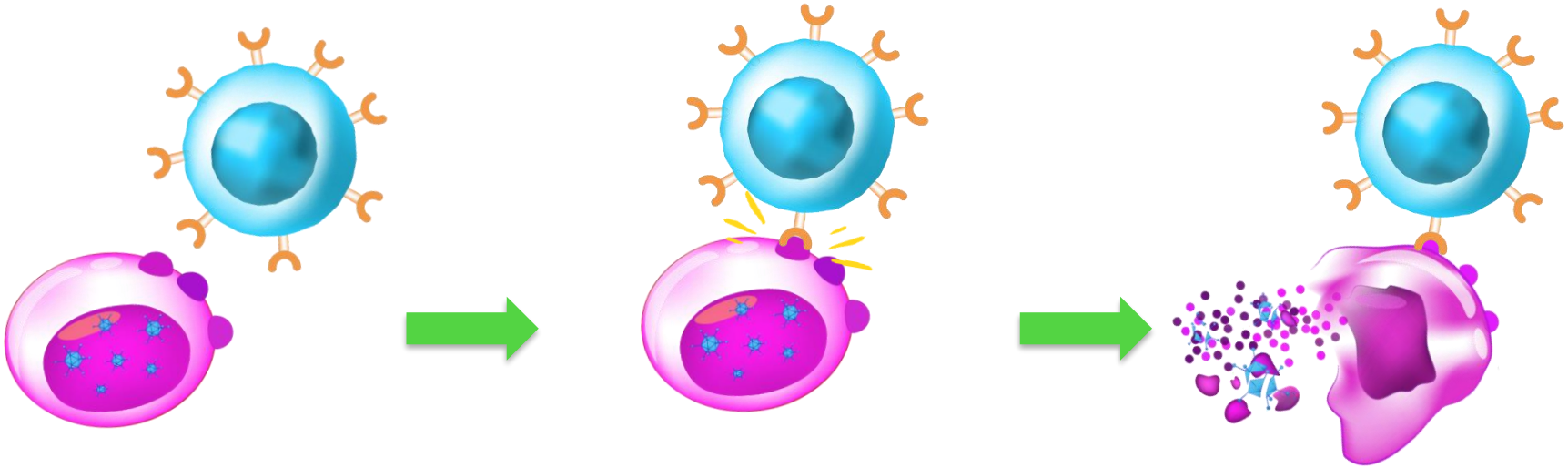
T-cell receptor can recognise surface protein (antigen) of infected cell

2

T-cell receptor binds to the antigen

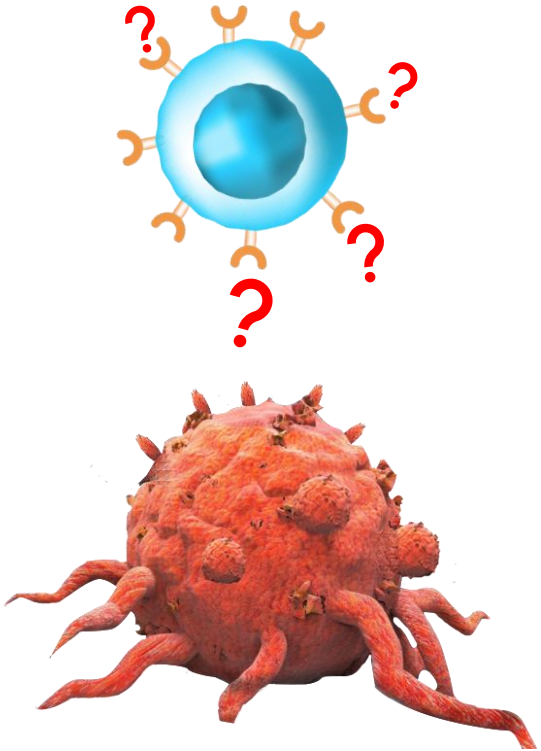
3

T-cell activates and kills the infected cell



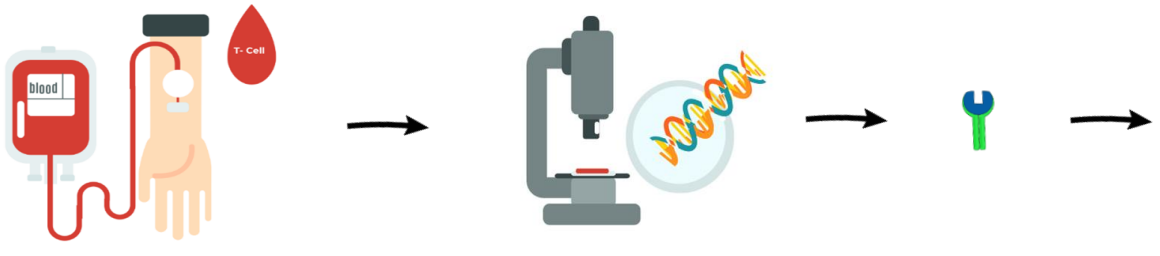
Why can’t our T-cells see cancer cells?

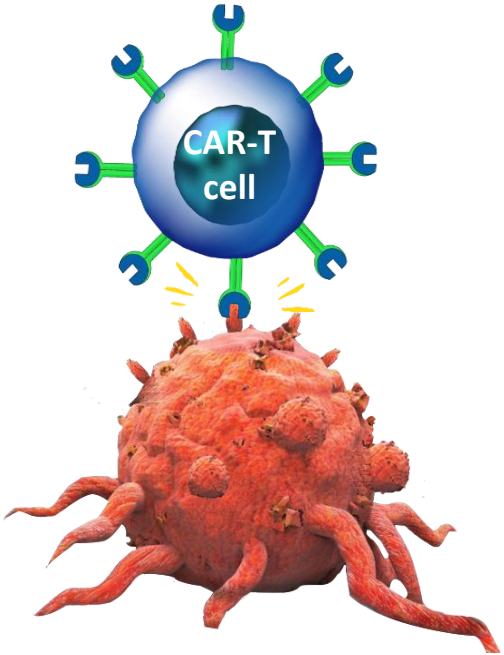
- Cancer has learned to evade our immune system by changing the antigens on its surface
- Without the right receptor, T-cells **cannot identify cancer cells**



…so how do you reprogram a T-cell to recognise and kill cancer cells?

...by adding a cancer receptor to the T-cell!





- A new receptor that can recognise a cancer antigen is added to a patient's own T-cells
- The resultant cell is a "chimera": the patient's T-cell + an engineered receptor
- Chimeric Antigen Receptor T-cell or "CAR-T cell" - can now recognise and kill the cancer cells.

How does the CAR-T process work?

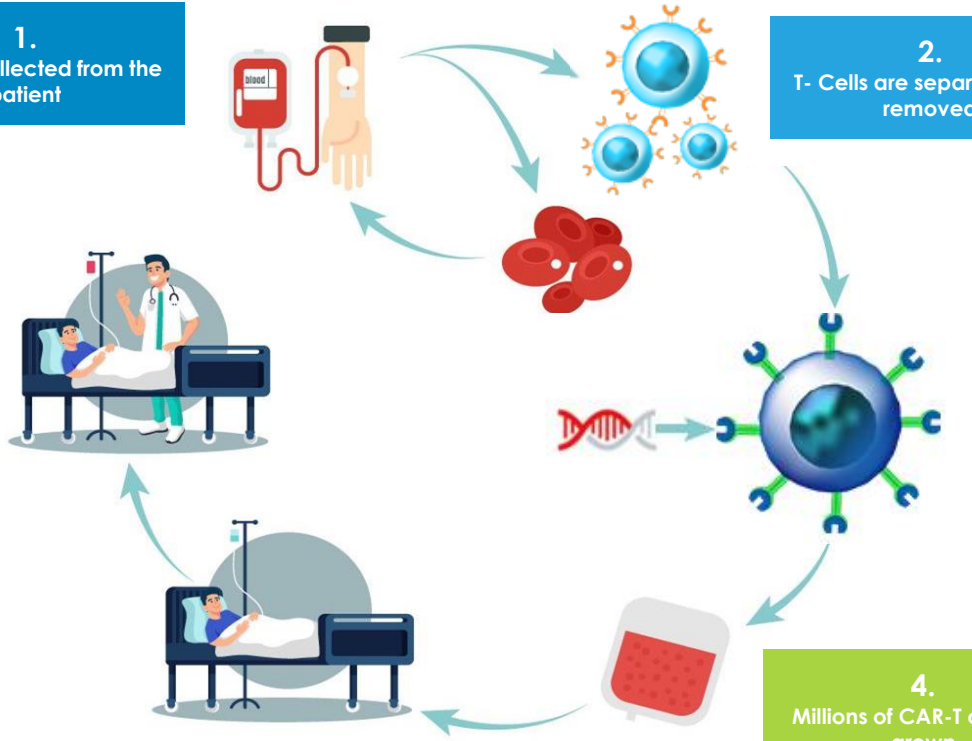
1.
Blood is collected from the patient

2.
T- Cells are separated and removed

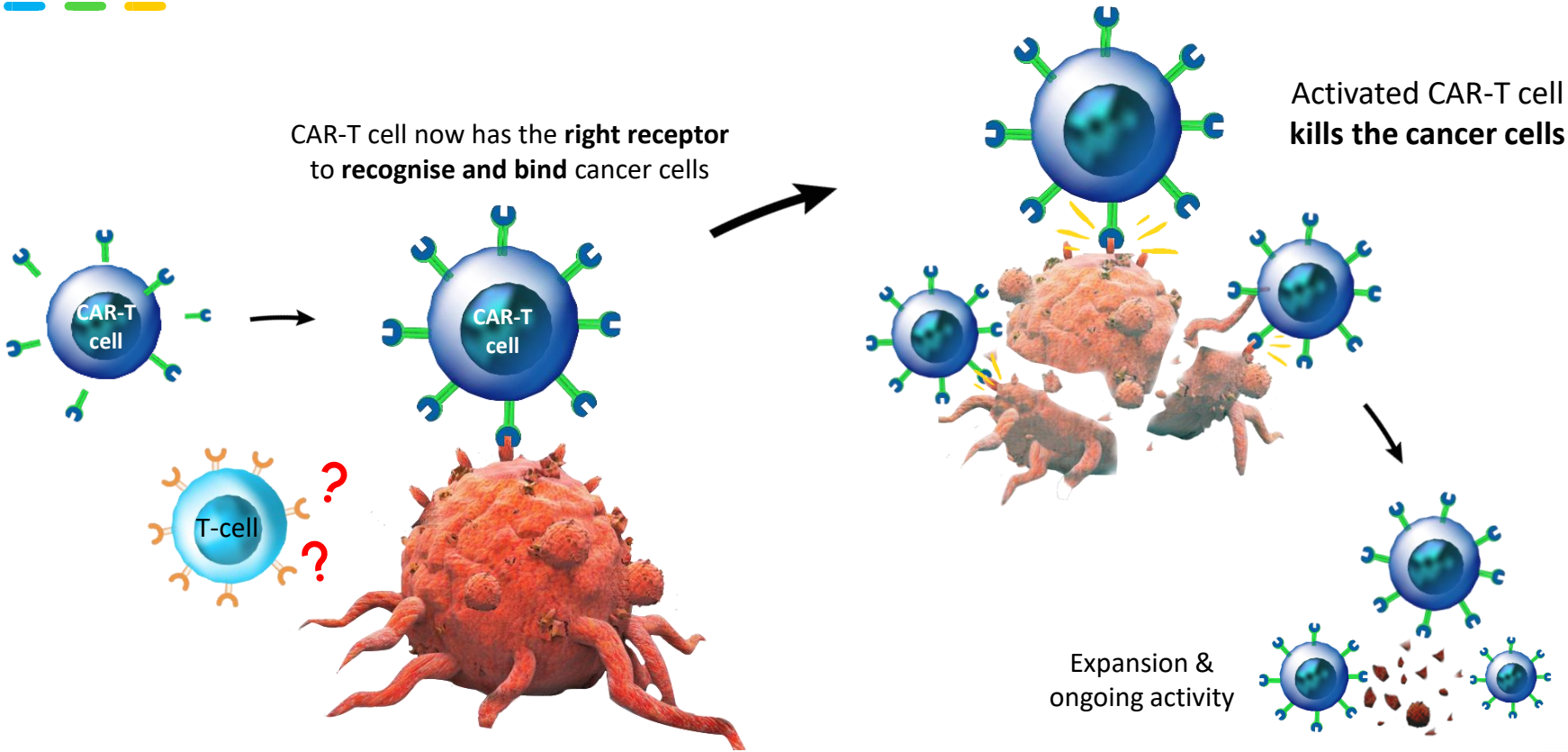
3.
T-Cells are genetically altered to have special cancer-recognising receptors called Chimeric Antigen Receptor (CAR)

4.
Millions of CAR-T cells are grown

5.
Patient first receives Chemotherapy, and then the CAR – T cells are delivered to the patient



CAR-T cells are now transformed into cancer killers



CAR-T therapies approved and in use

NOVARTIS

Licensed from **UPenn**

Cost of treatment per patient:
US$475,000
(A$730,000)

GILEAD Kite A GILEAD Company

Cost of treatment per patient:
US$373,000
(A$574,000)

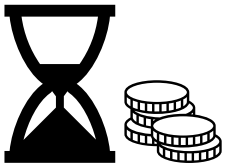
CAR-T deal activity

CAR-T has had stunning success, but…

- CAR-T has had spectacular and unprecedented success in treating certain types of blood cancers
  - **~80% response rates** in certain B cell lymphomas
- The field is now grappling with replicating CAR-T's success in other cancers
- However, there are substantial challenges…

Cleveland Clinic, 2020

What is holding back the field of CAR-T?



Time and Cost

of delivering treatment

Safety

CAR-T can have serious safety concerns

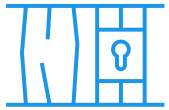
No Control

Clinicians have no control of cells post infusion

Targets

Finding targets that work;

Antigen heterogeneity (multiple targets) - esp. in solid tumours



Escape

Antigen loss leads to relapse

ENORMOUS OPPORTUNITIES FOR THOSE WHO CAN SOLVE THESE LIMITATIONS!

Prescient Therapeutics

Imagine what could happen to the *ENTIRE FIELD* if even some of these limitations were solved?

Imagine if CAR-T could *work just as well for other cancers* – including solid cancers?

Introducing the OmniCAR platform

- Pre-clinical universal, **modularised CAR-T** platform
- Potential best-in class universal immune receptor (UIR)
- Multi-disciplinary technology licensed from **UPenn**, world renowned for its pioneering and leadership in CAR-T
- Prescient granted exclusive world-wide rights
- Only UIR system with post-translational covalent binding
- Unique, powerful and flexible

Co-inventors

Associate Professor
Daniel J. Powell, Jr

Professor
Andrew Tsourkas

Powell, DJ et al, JACS; 2020

OmniCAR can do what conventional CAR-T cannot

Conventional CAR-T

- Soldier with only one map
- Single weapon
- Only trained to hit one target
- Incapable of redirection
- No communication or control in the field

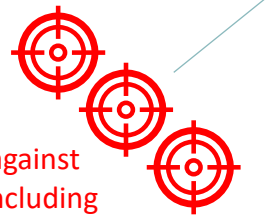
OmniCAR

Armed with **any weapon**

Including **several** at once

Can be given **any map**;
Multiple deployments

Full **communication** and **control** at all times, even mid-mission

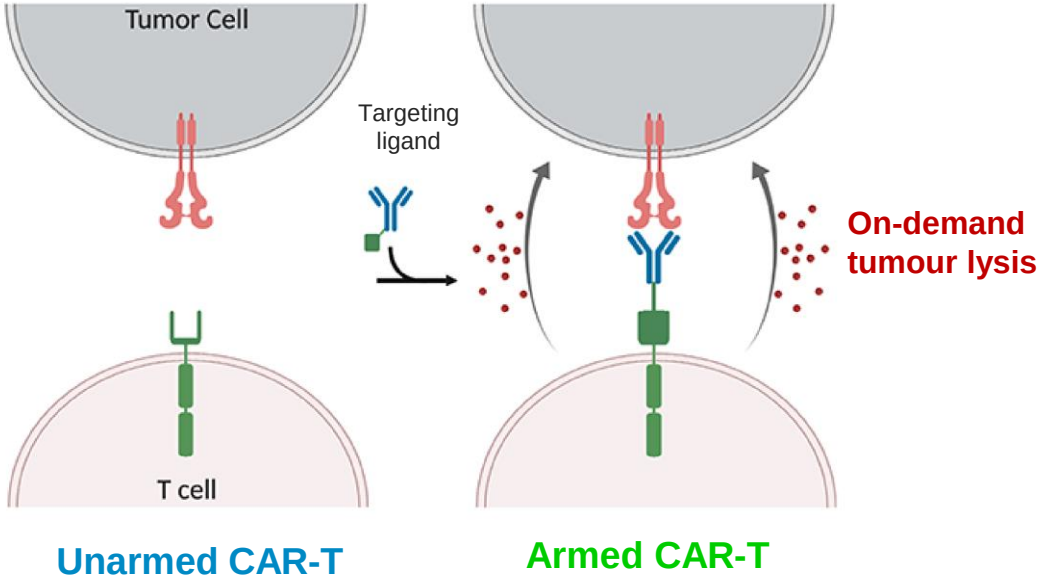


Can direct against **any target**, including **simultaneous** targets

Send **images** back to base in real time

How OmniCAR works

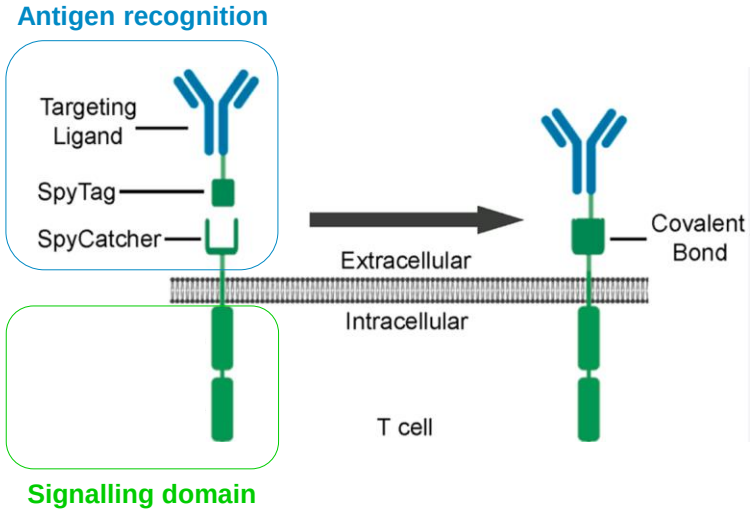
- Unarmed (and inactive) CAR-T cells are administered to patient
- Separate administration of targeting ligand results in a complete, armed CAR-T cell
- Armed CAR-T cells are activated, resulting in on-demand tumour killing
- CAR-T cell activity is **now controllable**
- Target specificity CAR-T cell can be switched at will, by administering a different targeting ligand



Powell, DJ et al, JACS; 2020

An elegant and effective approach

- Innovative SpyCatcher/SpyTag binding system separately licensed from **Oxford University**
- Decouples antigen recognition from signalling domains
- Switch specificity of the CAR-T cell from one target to another
- Only universal system with covalent loading of targeting ligands, conferring **advantages to other universal approaches**
- OmniCAR can utilise any type of targeting ligand:
  - scFv
  - Antibody
  - Aptamers
  - Labels for imaging



Adapted from Powell, DJ et al, JACS; 2020

Overcoming Clinical Limitations of CAR-T

Clinical Challenges	Conventional CAR-T	Universal CAR-T (OmniCAR)
On-demand activation of CAR-T cell	✘	✓
Controlling CAR-T cell activity post infusion	✘	✓
Control serious side effects (TLS; CRS)	✘	✓ (preventative and responsive)
Ability to terminate activity in the event of serious adverse event	✘	✓
Prevention of B-cell aplasia (CD19)	✘	✓ (reversible)
Recallable memory response	✘	✓
Solid tumour targeting	Off-target tissue activity is a major limitation	✓ Titrate to achieve therapeutic index
Addressing tumour antigen loss	✘	✓
Treatment of heterogeneous tumours	✘	✓
Universal vector design	✘	✓
Cost of therapy	High	Single vector design to reduce cost; can be incorporated into off-the-shelf T cells

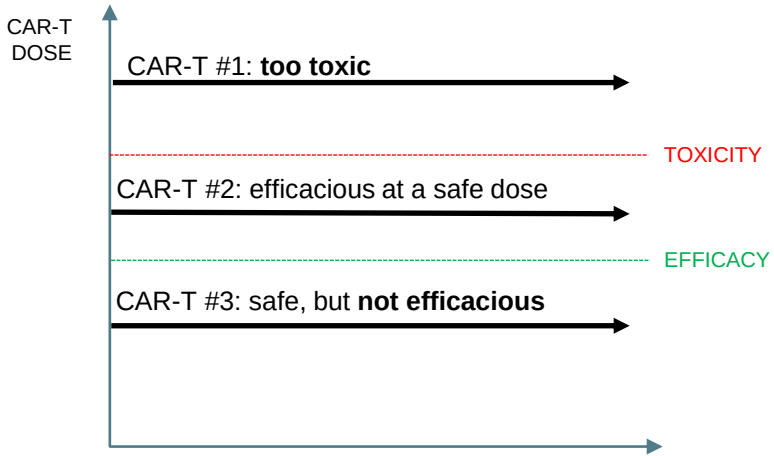
TLS: Tumour Lysis Syndrome
CRS: Cytokine Release Syndrome

Adapted from Travis Young PhD, California Institute for Biomedical Research, 2017

Safety: Ability Control Dose & Activity

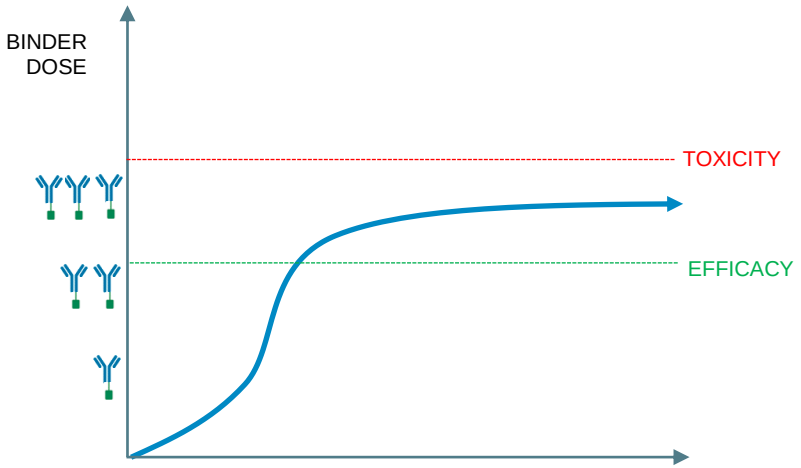
Conventional CAR-T

- Clinicians have **no control** over CAR-T activity once injected
- Balance between safety and efficacy can only be **estimated before infusion**



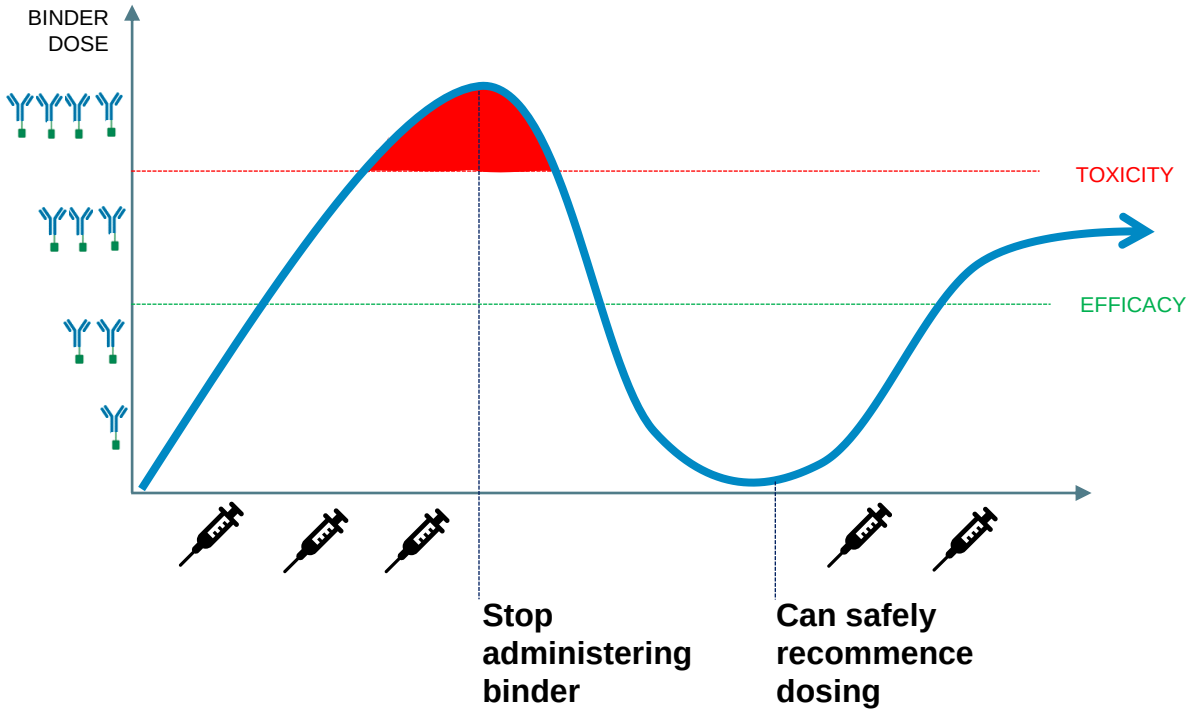
OmniCAR

- Clinicians have control **post infusion**
- Controlling subsequent **dose** of binder controls CAR-T **activity**
- Can titrate dose to **safe and efficacious** levels



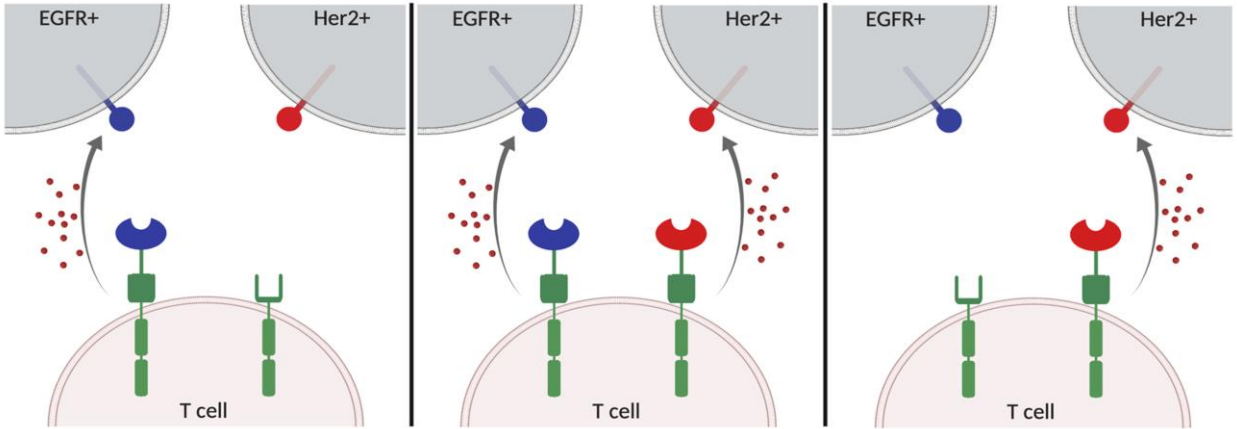
Safety: Built-in kill switch

- Conventional CAR-T cells cannot be switched off – a significant problem if toxicities arise
- OmniCAR activity can be **switched off at-will** by ceasing binder administration (or administering a blocking agent)
- Clinicians can **safely reactivate** CAR-T cell activity by recommencing binder administration



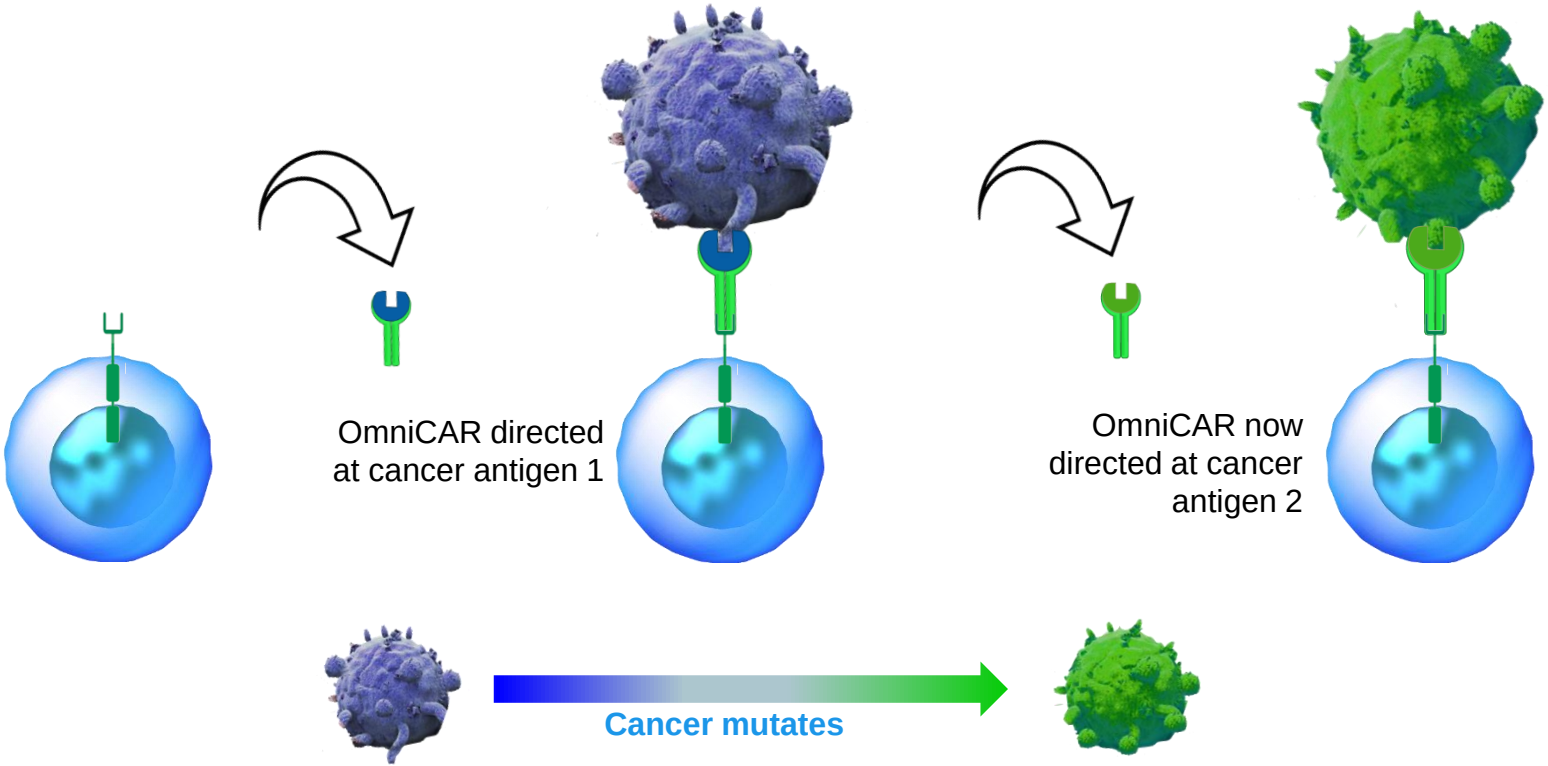
Multi-Antigen Capability with a Single Cell Product

- Ability to target **multiple cancer antigens** with a **single receptor, single cell product**
- Established proof of principal arming of OmniCAR against **several common tumour antigens**:
  - Her2
  - EGFR
  - EpCAM
  - CD20

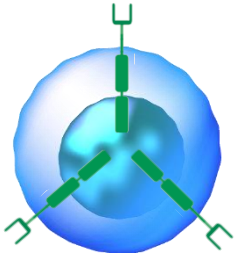


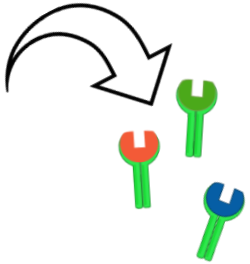
Powell, DJ et al, JACS; 2020

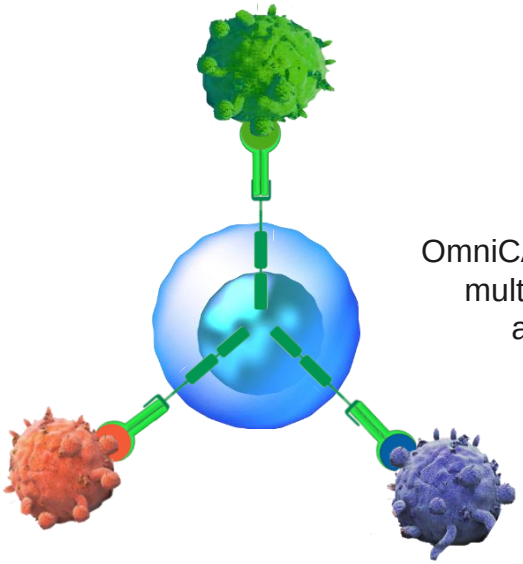
Ability to Target Multiple Antigens *Sequentially*



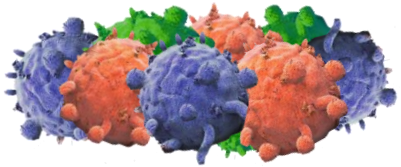
Ability to Target Multiple Antigens *Simultaneously*







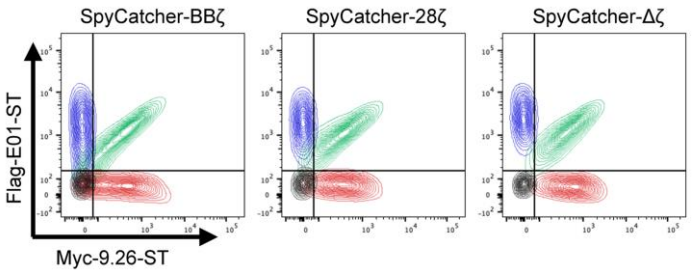
OmniCAR directed at multiple cancer antigens



Cancers with heterogenous antigens

Equal Arming & Equal Tumour Killing

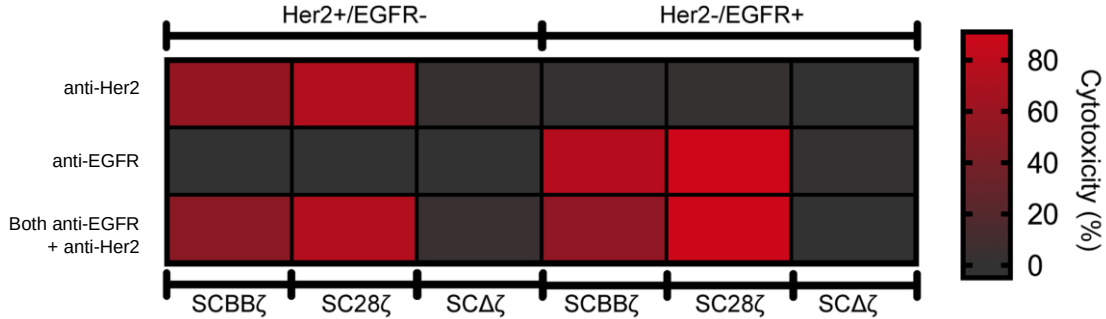
Equal arming



CAR-T equally armed with:

- Both anti-EGFR + anti-Her2
- anti-EGFR
- anti-Her2
- control

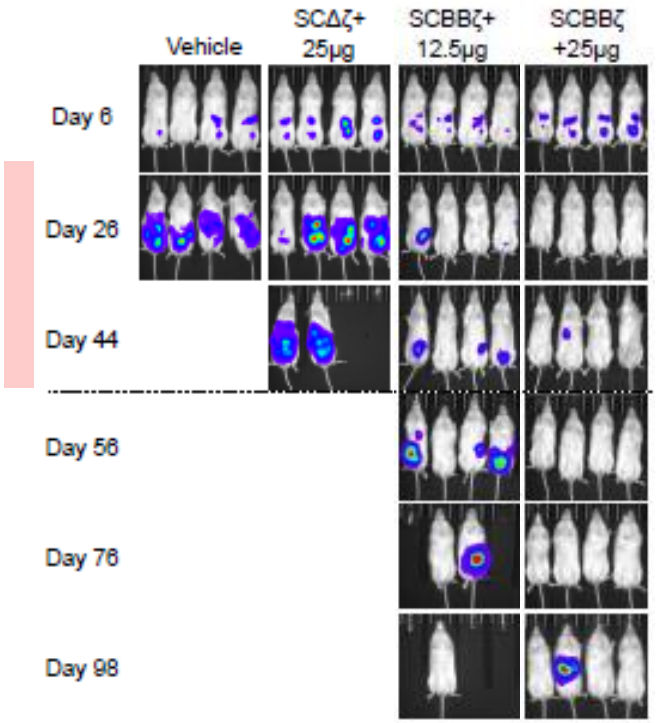
Specifically directed, at-will killing



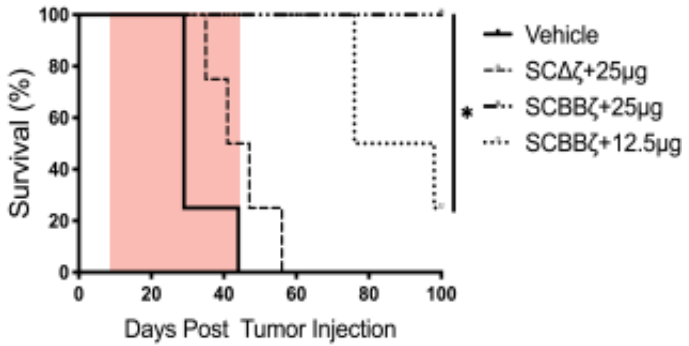
- **Only kills cells that the CAR-T is armed against**
- OmniCAR CAR-T cells have similar specific tumour killing capacity, whether **dual**-armed or **single**-armed

Powell, DJ et al, JACS; 2020

Control: Dose-dependent CAR-T activity!



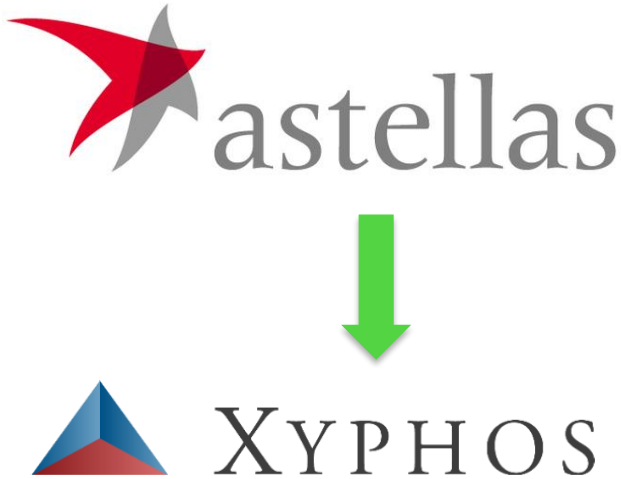
- Ovarian cancer model, targeting with anti-Her2 OmniCAR
- Loading more binder results in **proportionate killing** of cancer
- …and **proportionate survival**
- **Lasting effects** even when cease dosing of binder



Powell, DJ et al, JACS; 2020

= dosing window of binder

Value of a Universal CAR Platform



December 2019

- Astellas bought Xyphos Biosciences for **US$665M (US$120M upfront)**
- Xyphos was in **pre-clinical development** with their UIR system *convertible*CAR
- OmniCAR has several potential advantages

What else can OmniCAR do?

Potentially applicable to all cancer types

- Haematological cancers
- Solid cancers (a new frontier for CAR-T)

Other Applications

- Diagnostics
- Imaging of target tumour
- Autoimmunity

Improve many cell therapy approaches:

- Autologous T-cells (patient's own cells)
- Allogeneic T-cells (off the shelf cells)
- Producing enhanced versions of CARs with other cell types:
  - NK cells
  - Macrophage
  - T-reg cells
  - Stem cells

Parallel Development Strategy

IN HOUSE DEVELOPMENT

- Progress lead program
- Broaden OmniCAR platform
  - commercially attractive targets and applications
- Accommodated in current budget

EXTERNAL DEVELOPMENT

- Licensing
- Collaboration
- Improved versions of 3rd party CAR-Ts using OmniCAR
  - OmniCAR “Intel Inside®” model
- Non-oncology and non-therapeutic applications
- New product development off balance sheet
- Revenue potential

Presentation **Summary**

- ✓ **Transformational technology** from UPenn - the global leader in CAR-T
- ✓ Catapults PTX to the **forefront of CAR-T** development
- ✓ **Addressing the biggest problems** in the **most exciting area** of oncology
- ✓ An **enabling platform** not just for Prescient, but for **any other CAR-T player**
- ✓ Many development, collaboration and licensing possibilities!

ASX code: PTX

www.ptxtherapeutics.com

CONTACT

Steven Yatomi-Clarke
CEO & Managing Director
Prescient Therapeutics Limited
steven@ptxtherapeutics.com