Prescient Presents New Data Demonstrating Key OmniCAR Features for Predictable & Controllable CAR-T cell Therapy

Key points:

- **New OmniCAR pre-clinical data presented at Cell & Gene Meeting on the Mesa**
- **OmniCAR demonstrates key attributes including:**
  - **Dose-response of cancer killing activity and high potency;**
  - **Re-arming of OmniCAR-T cells;**
  - **Sequential arming to re-direct OmniCAR-T cells from one cancer antigen to another**

MELBOURNE Australia, 13 October 2021 – Prescient Therapeutics (ASX: PTX), a clinical stage oncology company developing personalised therapies to treat cancer, is presenting exciting new pre-clinical data on OmniCAR at the Cell & Gene Meeting on the Mesa in Carlsbad, California, the sector's foremost conference that brings together senior executives and decision makers on therapies including cell therapy. The new results demonstrate important capacilities of OmniCAR to deliver next generation cell therapies that are controllable and able to target multiple cancer antigens. These are important milestones not only in the development of Prescient's in-house OmniCAR programs, but in the development of the overall platform and demonstrating novel features relevant to potential partners and collaborators.

Prescient's Director of Scientific Affairs, Dr Rebecca Lim, said, "Critical features of OmniCAR have been tested in recent months and the data continue to be extremely positive. Our most recent work conducted in collaboration with the Peter MacCallum Cancer Centre showed that OmniCAR-T cells begin antigen-directed killing of tumour cells *in vitro* as soon as they are armed. The team also showed that OmniCAR-T cells could be re-armed and continue to kill tumour cells without loss of cytotoxicity.

Excitingly, we saw for the first time the real-time 'switchability' of the OmniCAR system where the tumour killing ability of the OmniCAR-T cells could be redirected towards a different antigen through the addition of a different binder. These early wins are extremely encouraging, and we look forward to the next phase of pre-clinical testing where the OmniCAR technology will be put through its paces using gold standard cancer models."

Dose response

A dose response relationship is the correlation between the amount of drug given and the magnitude of response. In conventional pharmacology, dose responses are typically straightforward to establish, enabling clinicians to administer the appropriate dose for patients to achieve desired therapeutic outcomes. Typically, higher doses lead to greater effects.

In cell therapies such as CAR-T therapy, where living cells that continue to grow and divide are administered to patients, effects are considerably less predictable and controllable.

OmniCAR aims to combine the potent cytotoxicity of cell therapy with the control and predictability of a conventional drug.

To this end, Prescient treated glioblastoma multiforme (GBM) cells with OmniCAR-T cells armed with varying amounts of SpyTagged EGFRviii and Her2 binders to test whether different doses of binders resulted in commensurate levels of CAR-T activity.

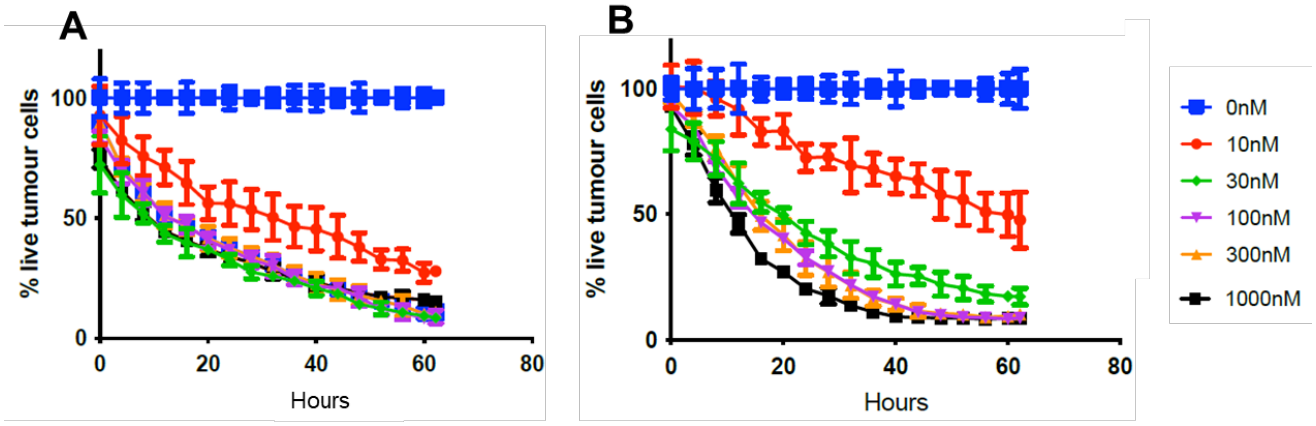


Figure 1: OmniCAR exhibits dose response with varying amounts of SpyTagged EGFRviii binders against GBM cells expressing EGFRviii (A); and also with varying amounts of Her2 binders against GBM cells expressing Her2 (B).

In both cases, OmniCAR exhibited dose-dependent tumour killing activity, with the ability to control OmniCAR-T cell activity commensurate with amount of binder administered (Figure 1).

Furthermore, this version of OmniCAR, employing version 3 of the SpyTag/SpyCatcher (ST/SC) system, demonstrated especially high potency, with 60-fold less binder required to exert the same cytotoxicity (in the low nM range) compared to version 1 ST/SC and other universal immune receptor systems. This is especially encouraging, as it has implications for further improving patient safety and lowering the cost of goods.

Re-arming

Single infusions of CAR-T cells may be insufficient to drive meaningful patient outcomes in many cancers, especially solid tumours. Whilst some CAR-T studies have demonstrated clinical efficacy in stubborn cancers with up to seven separate infusions of CAR-T cells, the time, cost, logistics and patient requirements of this approach is prohibitive. This is especially so in autologous CAR-T approaches.

In contrast, achieving ongoing control of T cell activity through complete control of binder administration is viable, logistically undemanding and inexpensive. Moreover, this method is identical to infusions of biological therapeutics used routinely in clinical practice today.

Prescient has now demonstrated this "re-arming" capability of OmniCAR. OmniCAR-T cells pre-armed with Her2 binders demonstrated potent ability to kill cancer cells expressing Her2. The cells were then washed and rested for seven days, resulting in unarmed OmniCAR cells.

These same OmniCAR-T cells were then capable of being re-armed with Her2 binders, and once again demonstrated targeted killing (Figure 2).

Not only were re-armed OmniCAR-T cells capable of antigen directed killing, but re-armed cells exhibited the same levels and kinetics of cytotoxicity of pre-armed OmniCAR-T cells.

This demonstrates that OmniCAR cells can be unarmed, re-armed and still kill with near identical fidelity. It is another example of the flexible yet predictable activity of OmniCAR cells.

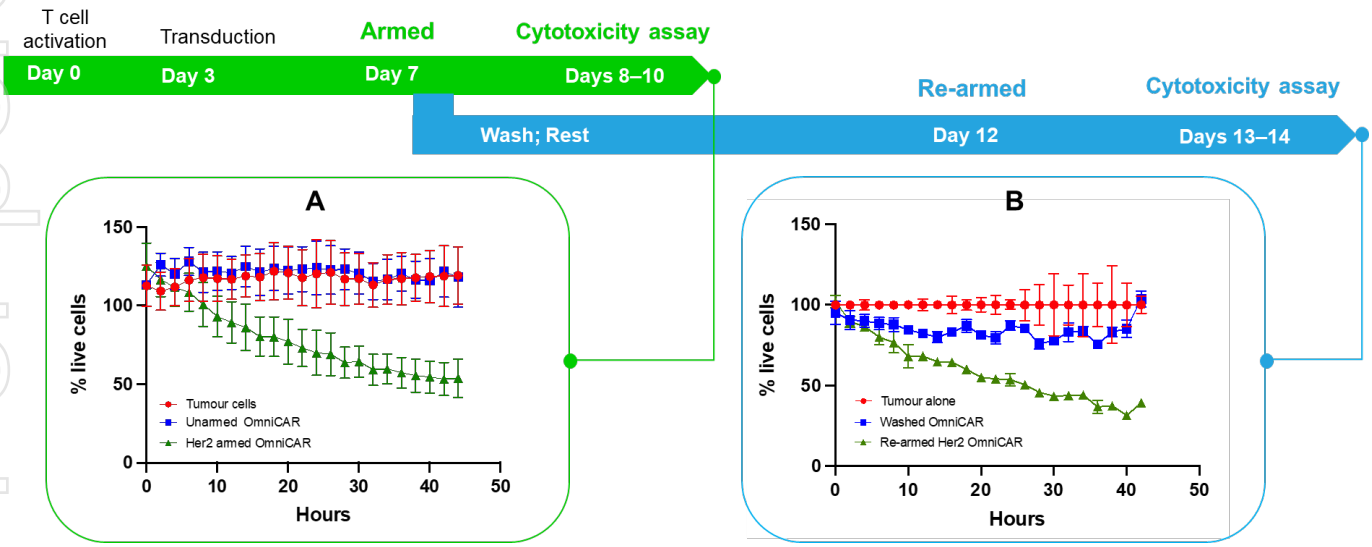


Figure 2: OmniCAR pre-armed with Her2 binders kills Her2 expressing tumour cells (A), can be unarmed, rested then re-armed with Her2 binders to exert equal cytotoxicity (B).

Sequential arming and re-direction

GBM is a brain cancer characterised by antigen heterogeneity and rapid mutations that drive rapid progression of disease. These characteristics present significant challenges for therapies, including CAR-T therapies, that rely on single antigen targeting.

Prescient is seeking to overcome these limitations with the development of OmniCAR to enable multi-antigen targeting. Prescient has now demonstrated a unique feature of OmniCAR to redirect a single cell product from one cancer antigen to another in GBM cells.

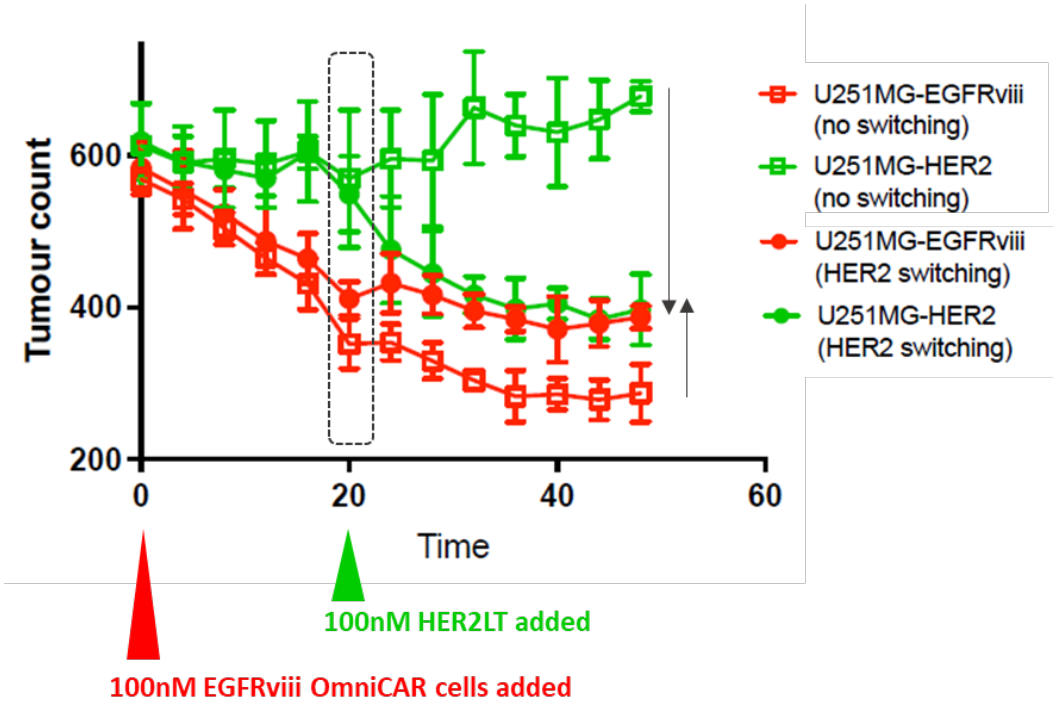
In a novel experiment, OmniCAR was tested sequentially against a co-culture of GBM cells expressing antigens Her2 or EGFRviii.

OmniCAR-T cells pre-armed with EGFRviii binders demonstrated rapid cytotoxicity against those GBM cells expressing EGFRviii.

Subsequent administration (at 20 hours) of Her2 binders (but without the need for additional T cells) demonstrated rapid switching of OmniCAR-T cells arming with Her2, and corresponding rapid cytotoxicity against Her2+ GBM cells.

This demonstrates that OmniCAR cells can be redirected to a different antigen target upon administration of a different SpyTagged binder without needing new cells. In each case, OmniCAR exhibited highly target tumour killing.

This highly novel feature will also be important in developing OmniCAR for acute myeloid leukemia (AML), which is another cancer characterised by high antigen heterogeneity, rapid mutations and rapid disease progression.



Prescient Managing Director and CEO Steven Yatomi-Clarke said, "We look forward to presenting this exciting data at Cell & Gene Meeting on the Mesa this week and next, where Prescient has the opportunity to share the features of OmniCAR with prominent companies in the field.

It is very pleasing to see a large body of work accomplished successfully so quickly and is a credit to the Prescient team and the incredible collaborators at Peter MacCallum Cancer Centre. Importantly, none of these tests have even been optimised, so we have yet to see the true limits of this technology. OmniCAR is proving to be a predictable and powerful system to work with. We look forward to sharing updates as our programs progress."

- Ends -

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About Prescient Therapeutics Limited (Prescient)

Prescient Therapeutics is a clinical stage oncology company developing personalised medicine approaches to cancer, including targeted and cellular therapies.

Cell Therapies

OmniCAR: is a universal immune receptor platform enabling controllable T-cell activity and multi- antigen targeting with a single cell product. OmniCAR's modular CAR system decouples antigen recognition from the T-cell signalling domain. It is the first universal immune receptor allowing post- translational covalent loading of binders to T-cells. OmniCAR is based on technology licensed from Penn; the SpyTag/SpyCatcher binding system licensed from Oxford University; and other assets.

The targeting ligand can be administered separately to CAR-T cells, creating on-demand T-cell activity post infusion and enables the CAR-T to be directed to an array of different tumour antigens. OmniCAR provides a method for single-vector, single cell product targeting of multiple antigens simultaneous or sequentially, whilst allowing continual re-arming to generate, regulate and diversify a sustained T-cell response over time.

Prescient is developing OmniCAR programs for next-generation CAR-T therapies for Acute Myeloid Leukemia (AML); Her2+ solid tumours, including breast, ovarian and gastric cancers; and glioblastoma multiforme (GBM).

Cell Therapy Enhancements: Prescient has several other initiatives underway to develop new cell therapy approaches.

Targeted Therapies

PTX-100 is a first in class compound with the ability to block an important cancer growth enzyme known as geranylgeranyl transferase-1 (GGT-1). It disrupts oncogenic Ras pathways by inhibiting the activation of Rho, Rac and Ral circuits in cancer cells, leading to apoptosis (death) of cancer cells. PTX- 100 is believed to be the only GGT-1 inhibitor in the world in clinical development. PTX-100 demonstrated safety and early clinical activity in a previous Phase 1 study and recent PK/PD basket study of hematological and solid malignancies. PTX-100 is now in a Phase 1b expansion cohort study in T cell lymphomas.

PTX-200 is a novel PH domain inhibitor that inhibits an important tumour survival pathway known as Akt, which plays a key role in the development of many cancers, including breast and ovarian cancer, as well as leukemia. Unlike other drug candidates that target Akt inhibition, PTX-200 has a novel mechanism of action that specifically inhibits Akt without non-specific kinase inhibition effects. This highly promising compound has previously generated encouraging Phase 2a data in HER2-negative breast cancer and Phase 1b in recurrent or persistent platinum resistant ovarian cancer, with a Phase 1b/2 trial currently underway in relapsed and refractory AML.

The Board of Prescient Therapeutics Limited has approved the release of this announcement.

Find out more at www.ptxtherapeutics.com or connect with us via Twitter @PTX_AUS and LinkedIn.

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Supplemental COVID-19 Risk Factors

Please see our website : Supplemental COVID-19 Risk Factors