Prescient Unveils CellPryme-A: Novel Adjuvant for Enhancing Cellular Immunotherapy

Key points:

- **CellPryme-A data unveiled at CAR-TCR Summit in Boston, MA – the world's largest CAR-TCR meeting**
- **CellPryme-A is an adjuvant that makes the tumour microenvironment more amenable to cellular immunotherapy**
- **Significantly improves tumour killing and survival**
- **Strongly synergises with CellPryme-M**
- **Can be incorporated into existing cell therapy programs**
- **Ready for use in clinical trials, with GMP materials available to partners now**
- **Opportunities for external collaborations and applications in enhancing Prescient's own OmniCAR programs**

MELBOURNE Australia, 23 September 2022 – Prescient Therapeutics (ASX: PTX), a clinical stage oncology company developing personalised therapies to treat cancer, unveils a novel adjuvant/neoadjuvant named CellPryme-A. CellPryme-A is designed to be administered to cancer patients as an intravenous infusion in combination with cellular immunotherapy, such as CAR-T cell therapy, to address the hostile tumour microenvironment that cellular immunotherapies face. In animal models CellPryme-A reduces the number of suppressive regulatory T cells surrounding solid tumours that counteract the effectiveness of CAR-T and other cancer therapies. Whilst CellPryme-A demonstrated superior tumour killing and survival in pre-clinical studies, its effects were even greater when used together with Prescient's CAR-T manufacturing technology, CellPryme-M. This exciting new data was presented at the 7th Annual CAR-TCR Summit (Boston, MA), the world's pre-eminent forum in the CAR and TCR fields of cellular immunotherapy. CellPryme-A is now ready for clinical testing and can be incorporated into clinical studies of existing cell therapies. For Prescient this opens up another avenue for collaboration with external parties and potential commercialisation. CellPryme-A has been developed by Prescient in collaboration with the Peter MacCallum Cancer Centre (Peter Mac), with Prescient owning the resultant intellectual property, which is the subject of a patent application.

Executive Summary of CellPryme-A benefits:

- Enhances tumour killing by conventional CAR-T cells; especially strong benefits when used in conjunction with CellPryme-M
- Improved host survival
- Reduces problematic Treg cells by 66%
- Increases ability of T cells to penetrate solid tumours
    - Cytotoxic T cells by 400%
    - Helper T cells by 300%
- Dramatically increases ability of CAR-T cells to expand within the host
    - Doubles CAR-T cell expansion
    - When used in conjunction with CellPryme-M:
        - Cytotoxic T cells increased by 900%
        - Helper T cells increased by 600%

What is CellPryme-A?

CellPryme-A is an adjuvant/neoadjuvant that is envisaged to be administered to patients as an intravenous infusion either prior to, or shortly after commencing cellular immunotherapy, such as CAR-T cell therapy. CellPryme-A could be given either before or alongside the cellular immunotherapy. The objective of CellPryme-A administration is to counteract the hostile "cold" tumour microenvironment that is known to dampen the tumour killing ability of CAR-T cells and similar types of cellular therapy. This is achieved by reducing the numbers of suppressive regulatory T cells (Tregs) that infiltrate into the tumour. Tregs are some of the most immunosuppressive immune cells in the body. In autoimmune diseases, it is the loss or dysfunction of Tregs that results in autoimmunity – where the immune system becomes hyper-activated in the absence of Tregs. The opposite is true in cancer, where tumours can evade immune surveillance by recruiting Tregs to the tumour. Tregs can create an immunosuppressive environment that prohibits efficient tumour killing, through the release of immunosuppressive cytokines and alterations in metabolic demand.

CellPryme-A reduces the numbers of problematic Tregs in solid tumours

Using an immune-competent mouse model of HER2+ colon cancer (MC38 colon carcinoma) and a conventional HER2-targeting CAR-T cell therapy, twice-weekly administration of CellPryme-A reduced the numbers of Tregs per mg of tumour by two-thirds, after one week of treatment (**Figure 1**).

CellPryme-A significantly increases CAR-T cell penetration into tumours

CellPryme-A increased in CAR-T infiltration into the tumours. Specifically, there was a three-fold increase in CD4+ helper CAR-T cell and a four-fold increase in CD8+ cytotoxic CAR-T cells. These changes were not associated with changes to the CAR-T phenotype. CellPryme-A treatment on its own had no impact on T cell exhaustion. This suggests that CellPryme-A could work in synergy with CellPryme-M (**Figure 2**).

Synergy between CellPryme-A and CellPryme-M

The addition of CellPryme-A to CellPryme-M pre-treated CAR-T cells showed impressive and demonstrable synergies in the aggressive MC38 colon cancer model. Notably, only one animal in the group that received the combination of CellPryme-A and CellPryme-M pre-treated CAR-T cells had detectable tumour by day 15 (**Figure 3**).

CellPryme-A increases survival

Unsurprisingly, the combination of CellPryme-M pre-treated CAR-T cells and CellPryme-A also improved the predicted survival of these animals. Administration of conventionally manufactured CAR-T cells did not improve the probability of survival in this model. The addition of CellPryme-A alone extended this to day 28. The combination of CellPryme-M pre-treated CAR-T cells and CellPryme-A saw 4 out of 7 animals survive beyond the intended length of study (i.e. beyond day 30) **(Figure 4).**

CellPryme-A dramatically increases expansion of CAR-T cells *in vivo*

CellPryme-A doubled the numbers of CD8+ cytotoxic CAR-T cells in the spleen, which is a secondary lymphoid organ and known to be a site of CAR-T cell accumulation.

The greatest CAR-T cell expansion was seen when CellPryme-M pre-treated CAR-T cells were administered alongside CellPryme-A, where CD4+ CAR-T cells expanded more than 6-fold and CD8+ CAR-T cells expanded more than 9-fold. It is evident that these proprietary technologies can work synergistically to enable even conventional CAR-T cells to deliver an unprecedented level of potency in the setting of solid cancer (**Figure 5**).

Prescient's Senior Vice President of Scientific Affairs, Dr Rebecca Lim, said, "Solid tumours continue to pose challenges to CAR-T therapies. It is crucial that we address the immunosuppressive contributions of regulatory T cells as they significantly inhibit the efficacy of even the best-in-class

CAR-T cells. The synergies between CellPryme-A and our CellPryme-M platform, gives cellular immunotherapy the best chance at success based on these animal studies. I envision applications beyond CAR-T given that other modalities of cellular immunotherapies like NK cells and macrophages face the same challenges when it comes to the tumour microenvironment. Even the proposed *in vivo* manufactured cellular therapies will face challenges when it comes to a Treg-rich tumour microenvironment. CellPryme-A can help solve that".

Prescient Managing Director and CEO Steven Yatomi-Clarke said, "Prescient is delighted to finally unveil CellPryme-A, as a distinct but complementary addition to CellPryme-M, to expand our stable of cell therapy enhancements. Together with Prescient's next-generation CAR platform, OmniCAR, Prescient has placed itself enviably at the forefront of cellular immunotherapy by creating technologies that overcome the challenges facing the field. These challenges – which include targeting an array of antigens; post infusion control; cell exhaustion and a suppressive tumour microenvironment – simply must be overcome in order to bring this promising new class of therapies to more patients, and to conquer different malignancies. We now have a comprehensive suite of technologies to address all of these challenges."

"Moreover, CellPryme-A is the latest in a portfolio of platform cell technologies that can not only create innovative programs for Prescient, but are also enabling technologies that open up third party commercialisation opportunities. They can be utilised separately, or together for synergistic benefit, depending on the needs of a particular cell therapy program."

Clinical grade supply of CellPryme-A is currently available, together with robust regulatory documentation. With this compelling body of preclinical data and the GMP-ready status of CellPryme-A, Prescient will be seeking to license CellPryme-A, with or without CellPryme-M, to external parties for incorporation into their own cell therapy programs. Early discussions with potential collaborators have commenced. Prescient will also be seeking to incorporate CellPryme-A into its own OmniCAR programs, especially in solid tumours.

An explanatory investor presentation on CellPryme-A will be lodged next week, as well as a special investor briefing on CellPryme-M to be held on Tuesday 27th September at 12pm (AEST). Register for the briefing here.

Supplementary data:

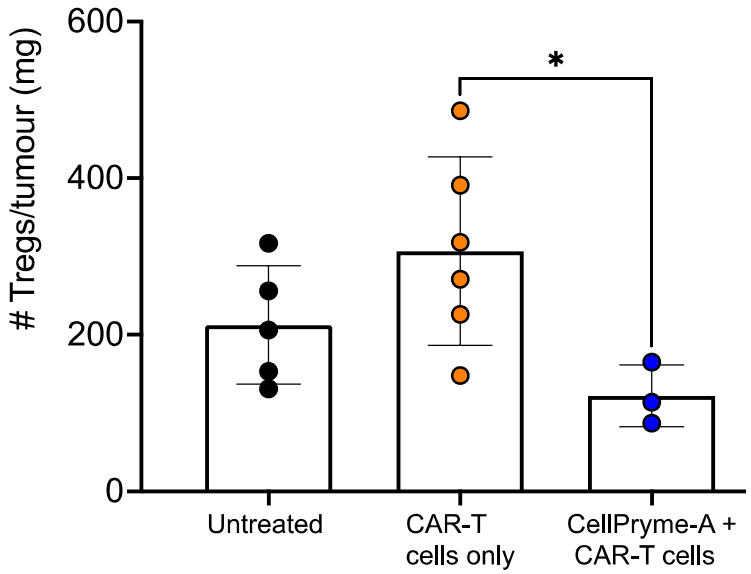

Figure 1. The numbers of intra-tumoural regulatory T cells (Tregs) following conventional HER2- CAR-T therapy was significantly reduced by two-thirds when CellPryme-A was included as adjuvant therapy (*p<0.05, Kruskal-Wallis one-way ANOVA).

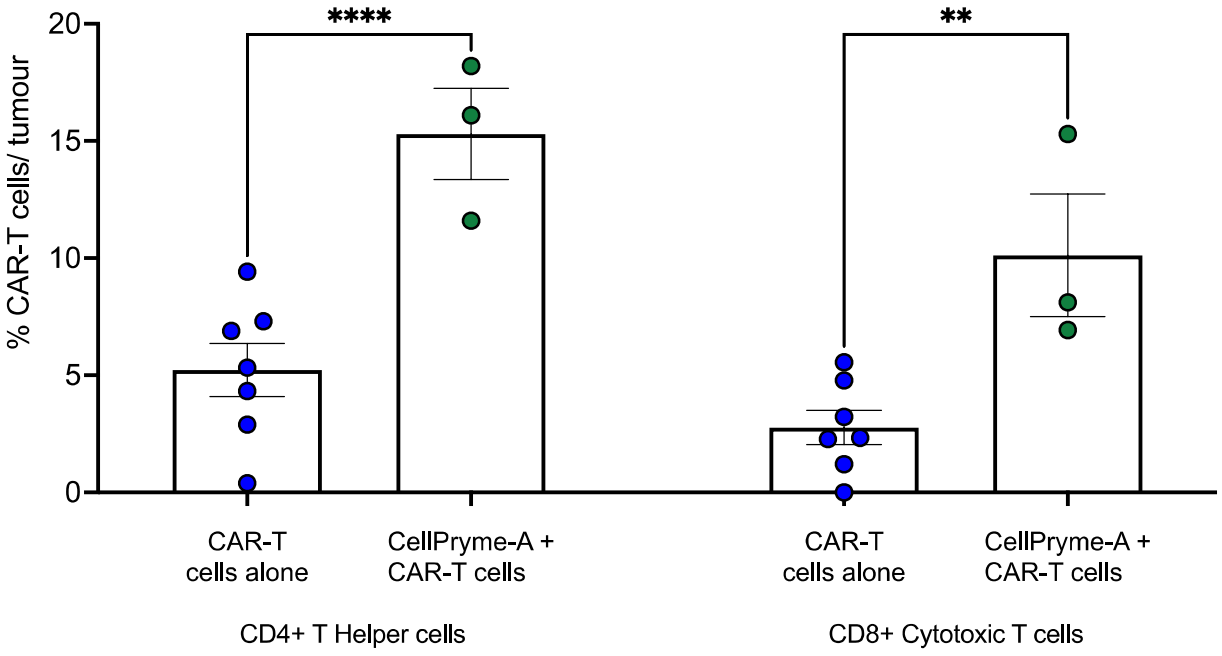

Figure 2. CellPryme-A adjuvant therapy increased the percentage of intratumoural CD4+ and CD8+ CAR-T cells by 3- and 4-fold respectively (p<0.01, ****p<0.0001, Mann-Whitney test).**

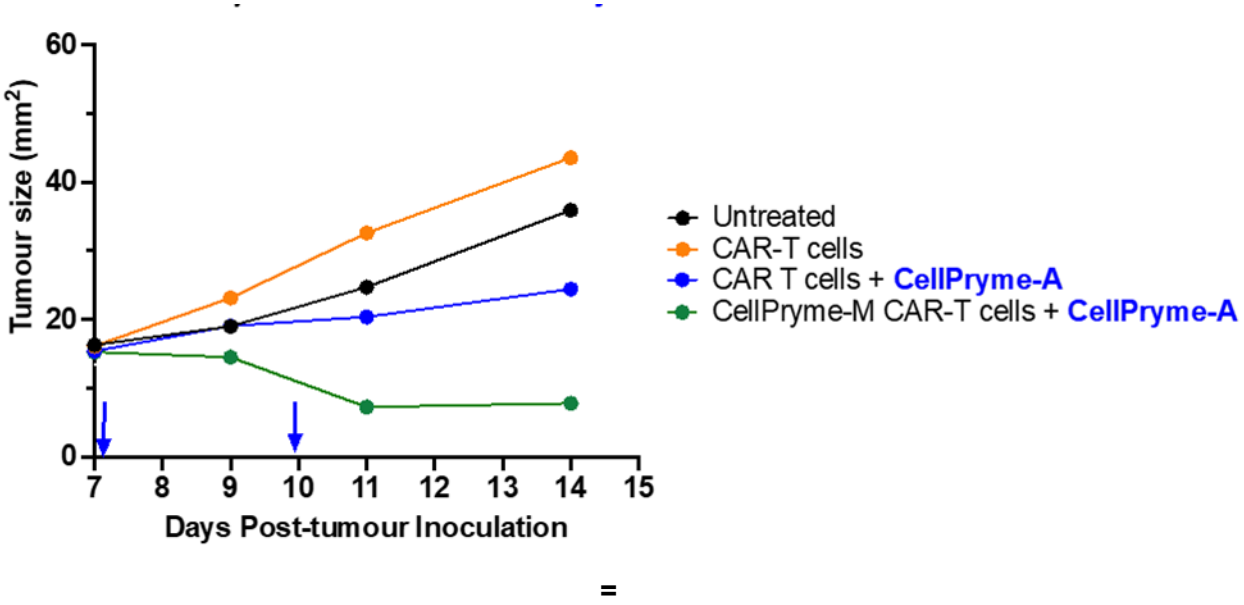

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Figure 3. Demonstrable synergies between CellPryme-A and CellPryme-M pre-treated CAR-T cells as shown in the tumour sizes in the MC38 model over time. The blue arrows indicate the timing of CellPryme-A administration. (*p<0.05, n=7 per group, two-way ANOVA, coloured areas indicate standard error of the mean).

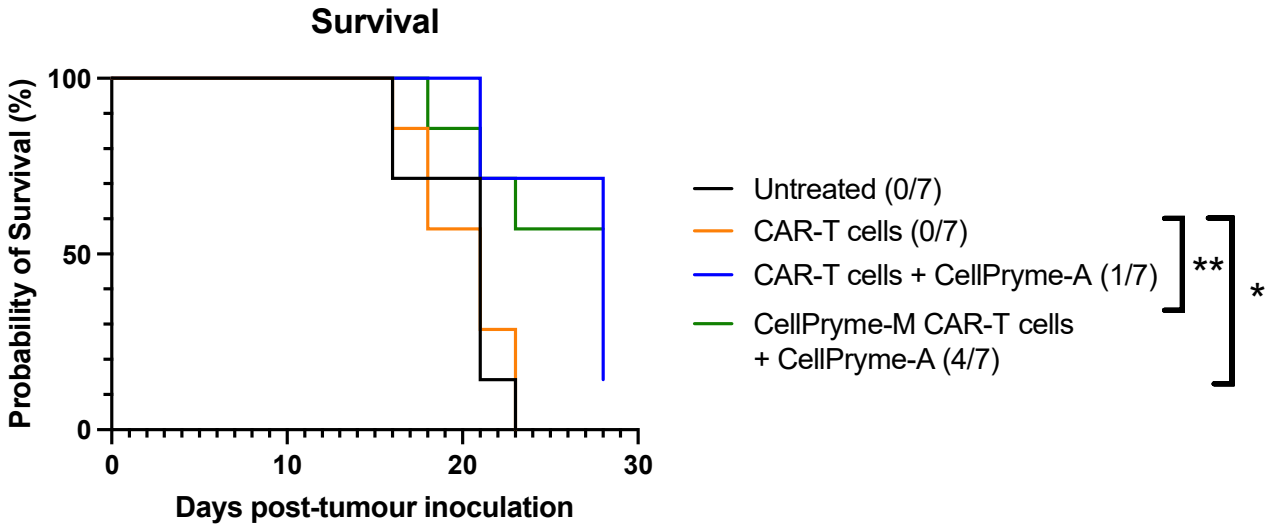

Figure 4. Survival curve showing the probability of survival across the different treatment groups. (*p<0.05, **p<0.001, Log-rank Mantel-Cox test).

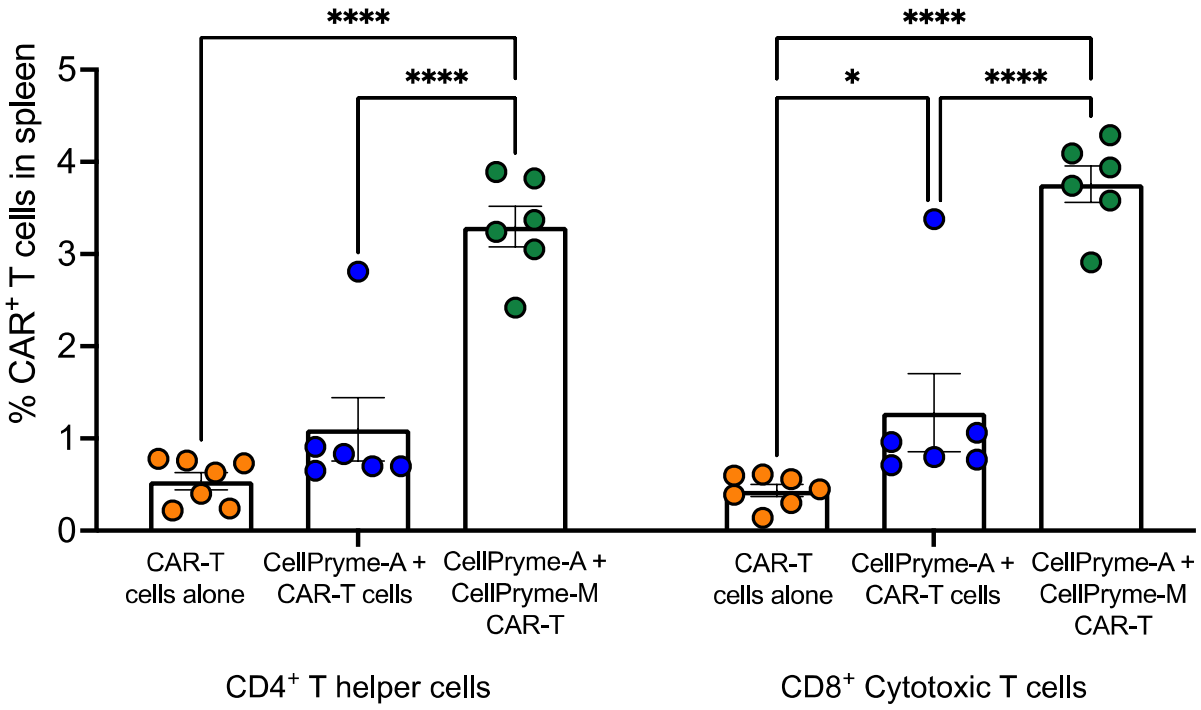

Figure 5. *In vivo* expansion of CD8+ CAR-T cells is increased by CellPryme-A co-administration but the most significant changes to CAR-T expansion is seen when CellPryme-A is given in combination with CellPryme-M pre-treated CAR-T cells. Both CD4+ and CD8+ CAR-T cells expand significantly when the two products are combined (*p<0.05, **** p<0.0001).

- 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).

CellPryme-M: Prescient's novel, ready-for-the-clinic, CellPryme-M technology enhances adoptive cell therapy performance by shifting T and NK cells towards a central memory phenotype, improving persistence, and increasing the ability to find and penetrate tumours. CellPryme-M is a 24-hour, non-disruptive process during cell manufacturing. Cell therapies that could benefit from additional productivity in manufacturing or increased potency and durability in-vivo, would be good candidates for CellPryme-M.

CellPryme-A: CellPryme-A is an adjuvant therapy designed to be administered to patients alongside cellular immunotherapy to help them overcome a suppressive tumour microenvironment. CellPryme-A significantly decreases suppressive regulatory T cells; increases expansion of CAR-T cells in vivo; increases tumour penetration of CAR-T cells. CellPryme-A improves tumour killing and host survival of CAR-T cell therapies, and these benefits are even greater when used in conjunction with CellPryme-M pre-treated CAR-T cells.

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, where it has shown encouraging efficacy signals and safety.

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 is currently in a Phase 1b/2 trial in relapsed and refractory AML, where it has resulted in 4 complete remissions so far. PTX-200 previously generated encouraging Phase 2a data in HER2-negative breast cancer and Phase 1b in recurrent or persistent platinum resistant ovarian cancer.

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.

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

Investor enquiries:
Sophie Bradley – Reach Markets
+61 450 423 331
ir@reachmarkets.com.au

Media enquiries:
Andrew Geddes – CityPR
+61 2 9267 4511
ageddes@citypublicrelations.com.au

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Supplemental COVID-19 Risk Factors

Please see our website : Supplemental COVID-19 Risk Factors