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# Development of targeted T-cell cancer immunotherapies based on a novel enantiomeric cationic lipid that promotes antigen cross-presentation and upregulation of type I interferons

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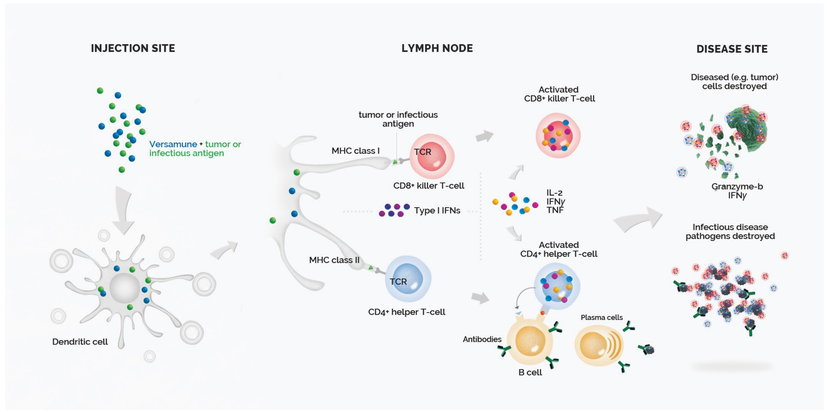
## VERSAMUNE® TECHNOLOGY

- The enantiomeric cationic lipid R-DOTAP nanoparticle platform (Versamune®) can promote efficient cross presentation of peptides/ protein antigens and upregulation of Type I interferons, leading to induction cytolytic polyfunctional CD8+ T-cells *in vivo. [1]*
- Versamune®- based immunotherapy containing human papilloma virus (HPV) derived antigens (PDS0101) was reported to induce high levels of antigen-specific cytolytic polyfunctional CD8+ T-cells *in vivo* and complete regression of TC-1 tumors in preclinical models. *[1]*
- In a Phase II trial (NCT04287868) of patients with HPV-related cancers who failed standard of care and received combination therapy with PDS0101, NHS-IL12 and bintrafusp alfa showed tumor shrinkage and improved patient survival. *[2,3]*

## VERSAMUNE® MECAHANISM OF ACTION




## METHODS

- To evaluate the potential efficacy of the Versamune® platform to treat non-viral associated cancer, we developed two immunotherapy formulations:
  - Versamune® based - TARP immunotherapy (PDS0102)
  - Versamune® based - MUC1 immunotherapy (PDS0103)
- To assess immunogenicity and biological activity, we injected human HLA-A2 expressing transgenic mice (AAD) with two doses of PDS0102 or PDS0103 formulations on day 0 and day 7 and characterized antigen-specific T cell-mediated immune responses induced by the vaccine formulations on day 14.

## VERSAMUNE®PLATFORM BASED IMMUNOTHERAPY FOR THE TREATMENT OF NON-VIRAL ASSOCIATED CANCERS

**Versamune® based - TARP immunotherapy (PDS0102)** platform contains long multi-epitope peptide antigens derived from the T-cell receptor gamma chain alternate reading frame protein (TARP), a tumor specific antigen overexpressed in prostate (~90%) and breast (~50%) cancers, as well as acute myelogenous leukemia (AML).

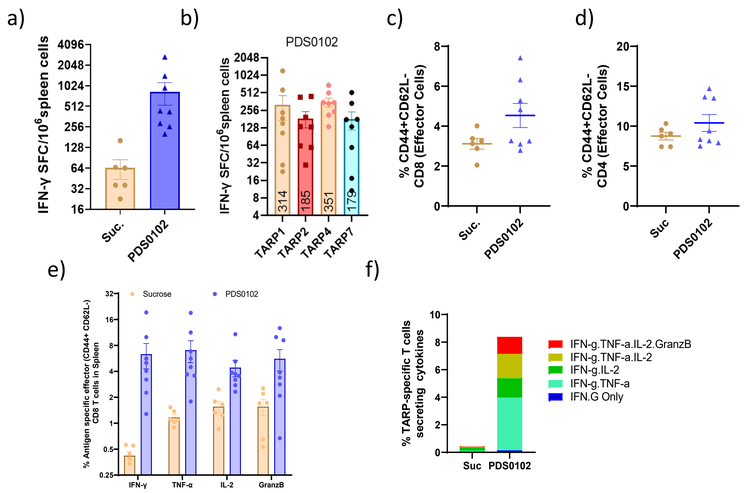



**Figure 1. PDS0102 induces a high number of antigen-specific and polyfunctional T-cells.** Antigen-specific T-cell responses in vaccinated mouse spleen were measured using mouse-IFN-γ ELISPOT assay and intracellular cytokine staining assay. IFN-γ producing T-cells in response to stimulation with a mixture of long peptides covering the entire 58 aa TARP sequence (a) or individual peptides consisting of verified HLA-A2 epitopes (b). Data represent effector cell percentages (CD44+ CD62L-) (c,d) and polyfunctional antigen-specific effector CD8+ T-cell percentages (e,f) in sucrose or PDS0102 vaccinated mice.

**Versamune® based - MUC1 immunotherapy (PDS0103)** platform contains multiple agonistic CD8+ T-cell epitope antigens derived from the extracellular and intracellular domains of human Mucin 1 (MUC1) protein, a tumor-associated antigen in a variety of epithelial cancers.

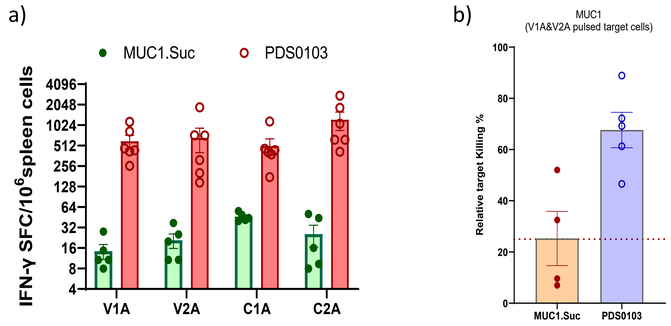



**Figure 2. PDS0103 induces a high number of antigen-specific CD8 T cells capable of killing cells presenting the human MUC1 derived peptides.** AAD mice were vaccinated on day 0 and day 7 with the PDS0103 formulation. On day 14, antigen- specific T-cell responses in vaccinated mouse spleens were measured by stimulating spleen cells with validated MUC1 derived HLA-A2 binding CD8+ T-cell epitopes (V1A, V2A, C1A and C2A) and measuring IFN-γ secretion in an ELISPOT assay (a). Cytotoxic activity of V1A- and V2A-specific CD8+ T-cells was measured by transferring V1A- and V2A-pulsed or control peptide pulsed spleen cells (1:1 ratio) and enumerating change in the ratio of V1A and V2A pulsed and control cells in the spleen (b).

## MAJOR FINDINGS AND FUTURE DIRECTIONS

- Versamune®-based nanoparticles formulated with tumor-derived antigens induced robust CD8+ and CD4+ T-cell responses. CD8+ T-cells induced by the Versamune® platform were polyfunctional and produced multiple cytokines (Fig 1), [*1*] capable of driving anti-tumor immune responses. CD8+ T-cells induced by the Versamune® platform were cytotoxic and are effective in identifying and killing cells presenting human MUC1-derived antigens (Fig 2).
- These results demonstrate the Versamune®-based T-cell activating platform's ability to generate effective anti-tumor immune responses. Further studies evaluating its potential in combination with checkpoint inhibitor therapy to promote anti-tumor immunity is ongoing.

References: 1. Antigen Priming with Enantiospecific Cationic Lipid Nanoparticles Induces Potent Antitumor CTL Responses through Novel Induction of a Type I IFN Response. Gandhapudi SK et al. J Immunol June 15, 2019, 202 (12) 3524-3536; DOI: https://doi.org/10.4049/jimmunol.1801634. 2. Phase II evaluation of the triple combination of PDS0101, M9241, and bintrafusp alfa in patients with HPV 16 positive malignancies. Strauss J et al. J Clin Oncol 39, 2021 (suppl 15; abstr 2501). DOI: 10.1200/JCO.2021.39.15_suppl.2501. 3. Phase II evaluation of the combination of PDS0101, M9241, and bintrafusp alfa in patients with HPV 16+ malignancies. Strauss J et al. J Clin Oncol 40, no. 16_suppl (June 01, 2022) 2518-2518. DOI: 10.1200/JCO.2022.40.16_suppl.2518.