



# ANV600, a *cis*-signaling $\alpha$ PD-1/IL-2R $\beta/\gamma$ agonist, expands both CD4<sup>+</sup> and CD8<sup>+</sup> tumor specific T cells by acting in the tumor microenvironment and draining lymph nodes

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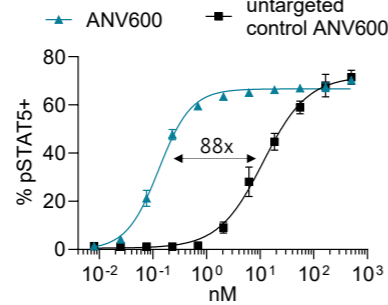
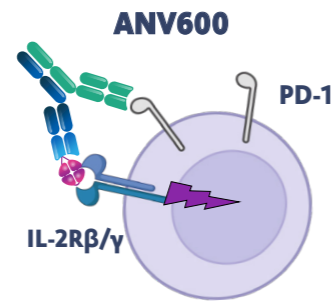
## Background

**ANV600 combines a unique non-blocking PD-1 targeting approach with an IL-2R $\beta/\gamma$  selective agonistic principle**

The cytokine bearing arm (blue) of the bispecific antibody is composed of IL-2 fused to an anti-IL-2 antibody, which sterically prevents IL-2R $\alpha$  from binding to the fusion protein. It therefore selectively signals through IL-2R $\beta/\gamma$ . The targeting arm (green) consists of a high affinity  $\alpha$ PD-1 antibody to selectively deliver ANV600 to tumor antigen experienced PD-1<sup>+</sup> T cells. The anti-PD-1 arm binds to a unique epitope on PD-1 that enables combination of ANV600 with PD-1 checkpoint inhibitors.

**ANV600 anchoring to PD-1 increases IL-2R signaling potency on PD-1<sup>+</sup> cells**

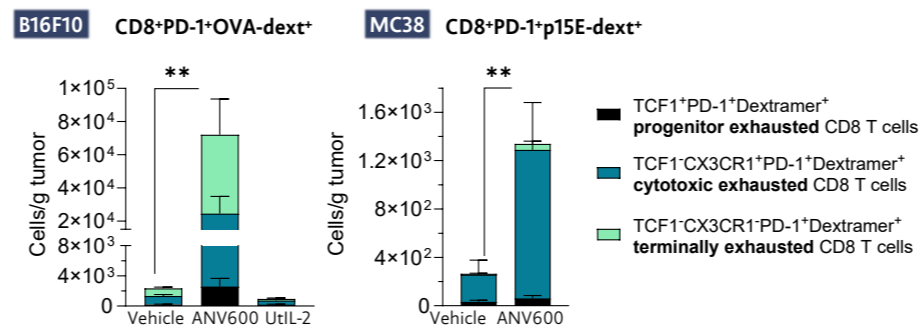
Potency measurements of STAT5 phosphorylation in PD-1<sup>+</sup> Jurkat T cells demonstrate a strong PD-1 targeting effect of ANV600. Compared to a non-targeted IL-2R $\beta/\gamma$  agonist control molecule, ANV600 has an 88-fold increased IL-2R signaling potency on PD-1 expressing cells.



## Results

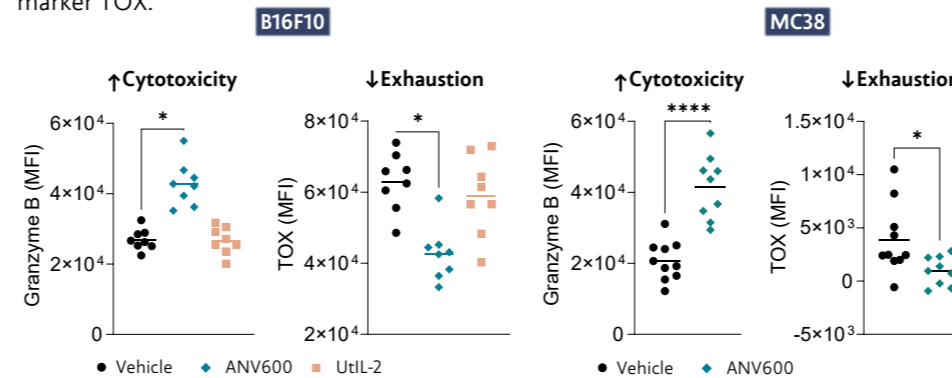
**ANV600 increases tumor antigen-specific CD8<sup>+</sup>PD-1<sup>+</sup> tumor infiltrating lymphocytes**

TILs analysis from tumor bearing hPD-1 transgenic mice reveals that ANV600 significantly expands CD8<sup>+</sup>PD-1<sup>+</sup>OVA-dextramer<sup>+</sup> cells in B16F10-OVA tumors and CD8<sup>+</sup>PD-1<sup>+</sup>p15E-dextramer<sup>+</sup> cells in MC38 tumors compared to vehicle or untargeted IL-2R $\beta/\gamma$  agonist (UtiL-2) treatment. This expansion is particularly pronounced in the cytotoxic exhausted T cell subset (T<sub>cehx</sub>), critical for potent anti-tumor responses.



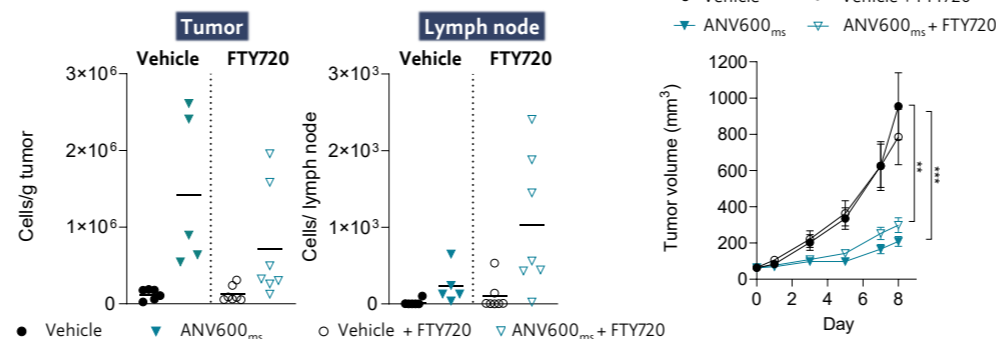
**Intratumoral T<sub>cehx</sub> cells are more functional and less exhausted after ANV600 therapy**

Upon treatment with ANV600, cytotoxic exhausted (T<sub>cehx</sub>) CD8<sup>+</sup> T cells in B16F10-OVA and MC38 tumors from hPD-1 transgenic mice exhibit higher Granzyme B expression, reflecting enhanced effector functionality, along with a reduction in the exhaustion marker TOX.



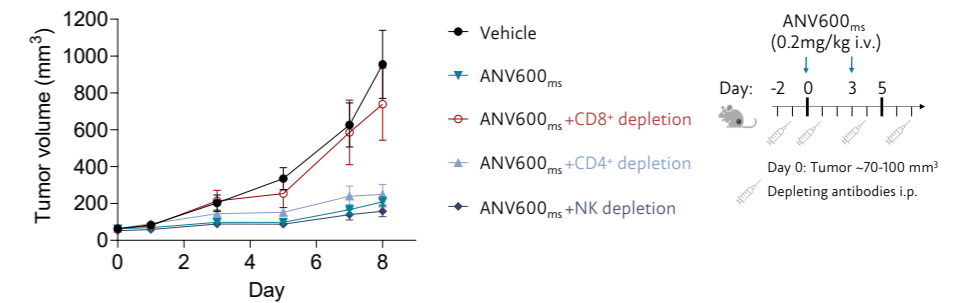
**ANV600 primarily amplifies cytotoxic exhausted CD8<sup>+</sup> T cells locally within the tumor**

In B16F10 tumor-bearing mice treated with ANV600 mouse surrogate (ANV600<sub>ms</sub>), blockade of T cell egress from lymph nodes with FTY720 partially reduces the number of cytotoxic exhausted (T<sub>cehx</sub>) CD8<sup>+</sup> T cells in the tumor and increases their retention in the draining lymph nodes. Despite FTY720 treatment, ANV600<sub>ms</sub> maintains anti-tumor efficacy, suggesting that its therapeutic effects are primarily driven by localized action in the tumor rather than systemic lymphocyte trafficking.



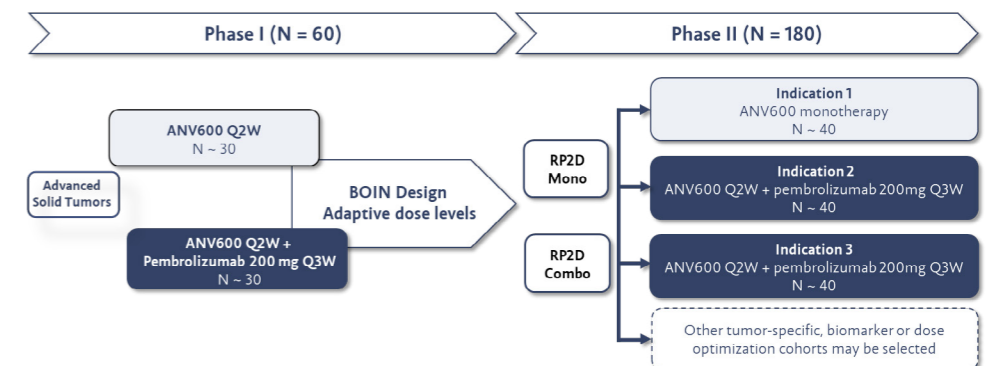
**Anti-tumor activity of ANV600 relies on CD8 T cells**

In the B16F10 tumor model, depletion of CD8<sup>+</sup> T cells abolishes the tumor growth inhibition induced by ANV600<sub>ms</sub>, leading to significant tumor progression. In contrast, depletion of CD4<sup>+</sup> T cells or NK cells has a minor impact on the therapeutic efficacy of ANV600<sub>ms</sub>, as tumor growth remains suppressed in these groups. These results further highlight that CD8<sup>+</sup> T cells are the primary mediators of ANV600 anti-tumor efficacy.



**ANV600 is currently tested in the Phase I/II clinical trial EXPAND-1 (NCT06470763)**

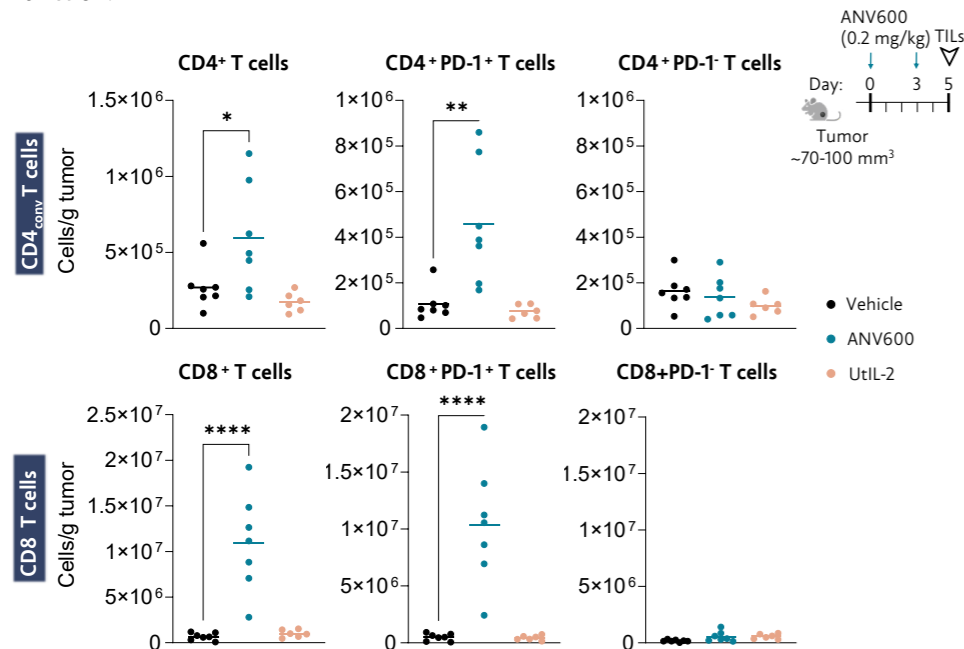
The purpose of study ANV600-001 is to characterize the safety, tolerability, pharmacokinetics, pharmacodynamics, immunogenicity and antitumor activity of ANV600 administered as a single agent or in combination with pembrolizumab in adult participants with advanced solid tumors.



## Results

**ANV600 preferentially expands tumor infiltrating CD8<sup>+</sup> PD-1<sup>+</sup> and CD4<sup>+</sup> PD-1<sup>+</sup> T cells**

Compared to an untargeted IL-2R $\beta/\gamma$  agonist (UtiL-2), treatment of subcutaneous (s.c.) B16F10 tumor bearing human PD-1 (hPD-1) transgenic mice with ANV600 induces expansion of intratumoral CD8<sup>+</sup> and CD4<sup>+</sup>Foxp3<sup>-</sup> (CD4<sub>conv</sub>) T cells, which is mainly driven by the effect on the PD-1<sup>+</sup> subsets. The increase in CD4<sub>conv</sub> PD-1<sup>+</sup> T cells suggests that ANV600 not only enhances cytotoxic T cell activity but also promotes helper T cell function.



## Conclusions

- ANV600 is a PD-1 targeted IL-2R $\beta/\gamma$  agonist combinable with PD-1 blocking checkpoint inhibitors.
- ANV600 preferentially expands tumor-infiltrating PD-1<sup>+</sup> CD8<sup>+</sup> and CD4<sup>+</sup> T cells, supporting both cytotoxic T cell activity and helper T cell function, crucial for effective long-term anti-tumor immunity.
- ANV600 amplifies tumor antigen-specific T cells in the B16F10-Ova and MC38 s.c. tumor models, especially within the cytotoxic exhausted CD8<sup>+</sup> T cell (T<sub>cehx</sub>) subset.
- The anti-tumor efficacy of ANV600 is primarily driven by localized action in the tumor and depends on the CD8<sup>+</sup> T cell immune response.
- A Phase I/II clinical trial (NCT06470763) has been initiated to evaluate the safety and efficacy of ANV600 in cancer patients as monotherapy and in combination with pembrolizumab.

