ANTIBODY (nM)

**Introduction: Inhibitory Checkpoints Down-Modulate Immune Responses**

- Inhibitory checkpoint receptor-ligand interactions are essential for down-regulating immune responses and maintaining self-tolerance.
- Functional antagonist antibodies to PD-1 and CTLA-4, major checkpoints on activated T cells, enhance existing immune responses and are approved therapeutics for immune-oncology indications.
- Genetic mutations in the PD-1 pathway have been shown to increase susceptibility to various autoimmune and inflammatory diseases.
- We hypothesize that many human autoimmune diseases occur due to dysregulated PD-1 signaling leading to uncontrolled T cell responses.
- Antibodies to PD-1 that mimic the function of natural ligands and augment PD-1 signaling have the potential to suppress human autoimmune/inflammatory diseases and reinstates tolerance.

**Anti-PD-1 Agonist Antibody Discovery**

An antibody (nM) is a human IgG1 antibody that binds to PD-1 and is highly specific and functional. We have observed that the antibody can block PD-L1 binding to PD-1, and it also induces SHP2 but not SHP1 recruitment to PD-1 after activation of Jurkat PD-1 cells.

**Kinase ExA Human PD-1**

<table>
<thead>
<tr>
<th>Kinase</th>
<th>Human PD-1</th>
<th>Cynomolgus PD-1</th>
<th>Mouse PD-1</th>
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<tr>
<td>Tyrosine Kinase</td>
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<td>CEP-09029</td>
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</table>

**ANB030 Binding to Human and Cynomolgus PD-1 is High Affinity**

A single 10 µg/mL dose of ANB030 was administered either intravenously or subcutaneously to biologic naïve non-human primates. ANB030 in nontoxic samples taken at various times after dosing was quantified by ELISA. Each protein is the mean serum concentration of ANB030 in 2 animals.

**Conclusions**

- Functional agonist anti-PD-1 antibodies that downregulate antigen-specific immune responses and lack antigen activity can be discovered and optimized.
- ANB030 is a humanized IgG1 anti-PD-1 agonist antibody that is non-immunogenic for PD-L1 binding and requires Fc receptor engagement for its biological activity in addition.
- ANB030 has been developed for preclinical development and is now advancing to clinical trials for the treatment of autoimmune and inflammatory diseases.
- In combination with anti-PD-1 and anti-CTLA-4 antibodies, ANB030 was able to synergize in vitro signaling, increased SHP2 recruitment with higher density ANB030 on the beads to Fc receptor engagement with variable ratios.
- In combination with therapeutic and immune checkpoint inhibition, ANB030 also reduced allo-M1 and N1 polarization (not shown).
- ANB030 induced PD-1 signaling in vitro that suppressed PD-1 expression in the absence of T cell activation (not shown).