Anti-PD-1×IL-10M Fusion Protein for the Treatment of Solid Tumors

Combining Modified IL-10 Monomer Variant and Anti-PD-1 Antibody

Overview

Drug Name	APD-IL10
Description	APD-IL10 is a first-in-class fusion protein that consists of a modified IL-10 monomer variant fused to an anti-PD-1 antibody. By reversing the exhausted CD8+ T cells in the tumor microenvironment, this fusion protein provides a promising therapeutic strategy for solid tumors refractory to anti-PD-1/PD-L1 therapy. In vivo studies, APD-IL10 showed a potent anti-tumor effect, good druggability, and good tolerability. An IND application for APD-IL10 is expected to be submitted to the FDA in early 2025.
Target	IL-10 and PD-1
Drug Modality	Fusion protein
Indication	Solid tumors
Product Category	Cancer immunotherapy
Mechanism of Action	Blocking PD-1 signaling and rejuvenating CD8+ T cells
Status	Preclinical
Patent	Granted

Collaboration Opportunity

Protheragen Inc. is actively seeking partnership for APD-IL10. Potential collaboration can be strategic alliance, licensing, or marketing agreement.
We look forward to hearing from you.

Target

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Interleukin 10 (IL-10)

Introduction	IL-10, a founding member of the IL-10 family of cytokines, is a noncovalent homodimeric α-helical cytokine with structural similarity to IFN-γ. IL-10 is encoded by the IL10 gene located on chromosome 1 and is primarily produced by regulatory T cells, B cells, macrophages, and dendritic cells. IL-10 is an immunosuppressive cytokine associated with a variety of regulatory or inhibitory immune-cell populations, such as regulatory CD4+ and CD8+ T cells, B10 cells, myeloid-derived suppressor cells, and tolerogenic dendritic cells, and it has a potent inhibitory effect on antigen presentation and immune-cell activation.
Approved Name	Interleukin 10
Official Symbol	IL10
Gene Type	Protein coding
Synonyms	CSIF; TGIF; IL10A; IL-10
Ensembl	ENSG00000136634
Gene ID	3586
Refseq	NM_000572
Protein Refseq	NP_000563
OMIM	124092
UniProt ID	P22301
Chromosome Location	1q32.1

Programmed Cell Death 1 (PD-1)

Introduction	PD-1 is a type I transmembrane receptor member of the immunoglobulin superfamily and is composed of 288 amino acids. PD-1 is predominantly expressed on activated T cells, B cells, NK cells, and activated monocytes in an immunosuppressive tumor microenvironment. PD-1 on the surface of immune cells binds to programmed death ligands on tumor cells, leading to negative regulation of the proliferation and activity of immune cells and facilitating tumor immune escape.
Approved Name	Programmed cell death 1
Official Symbol	PDCD1
Gene Type	Protein coding
Synonyms	CD279; PD1; hSLE1; PD-1

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Ensembl	ENSG00000188389
Gene ID	5133
mRNA Refseq	NM_005018
Protein Refseq	NP_005009
OMIM	600244
UniProt ID	Q15116
Chromosome Location	2q37.3

Drug Modality

Fusion Protein

APD-IL10 is a first-in-class biologic candidate combining modified IL-10 monomer variant (IL-10M) and an anti-PD-1 antibody. This fusion protein can deliver IL-10M to the exhausted T cells by targeting PD-1 in tumor microenvironment. The severe hematological toxicity of wild-type IL-10 limits its clinical application. The IL-10M of APD-IL10 is engineered from the dimer of wild-type IL-10, which has reduced hematotoxicity.

Indication

Solid Tumors

Solid tumors are abnormal mass of tissue that usually does not contain cysts or liquid areas. Solid tumors may be benign or malignant. Different types of solid tumors are named for the type of cells that form them, such as breast cancer, melanoma, hepatocellular carcinoma. Estimates from the International Agency for Research on Cancer (IARC) indicate that around 1 in 5 men or women worldwide develop cancer in their lifetime, while around 1 in 9 men and 1 in 12 women die from it. Solid tumors represent approximatively 90% of adult human cancers.

The commonly used treatment for cancer includes surgery, radiation therapy, chemotherapy, and some combinations of them. The best approach to treating cancer provides a balance between therapeutic

effectiveness and minimization of treatment-associated side effects. Immunotherapy offers new and precise treatment options and becomes the core pillar of cancer treatment. Immune checkpoint inhibitors are a major class of cancer immunotherapies and they have been identified as promising therapeutics capable of restoring tumor immunity in carefully selected patients.

Mechanism of Action

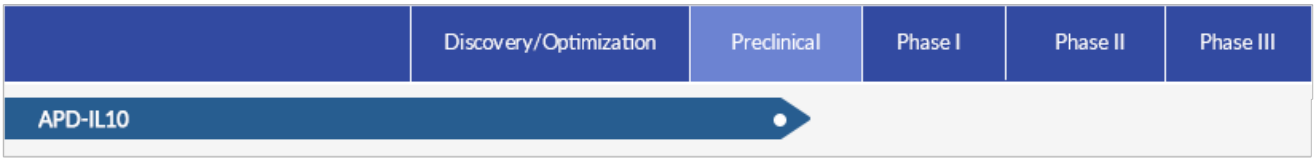
Blocking PD-1 Signaling and Rejuvenating CD8+ T cells

Both IL-10 and anti-PD-1 monoclonal antibodies target CD8+ tumor-infiltrating T cells (TILs), but their functional mechanisms are different. The antitumor effect of IL-10 may be the result of its stimulating activity on CD8+ T cells by promoting the differentiation and expansion of effector CD8+ T cells. Anti-PD-1 antibody removes the brake on antitumor cytotoxic T-cell lymphocyte killing by blocking the interaction between PD-1 and its ligand, thereby maintaining the antitumor immune activity of T cells.
As a unique biological agent, APD-IL10 is a fusion protein consisting of anti-PD-1 antibody and IL-10M. This combination delivers IL-10 specifically to antitumor CD8+ TILs, which improves the efficacy of both immunotherapeutic agents while avoiding the regulatory effect of IL-10 on off-target cells. In addition, IL-10M of APD-IL10 is a modified IL-10 monomer variant with attenuated IL-10 activity and deceased peripheral toxicity.

Status

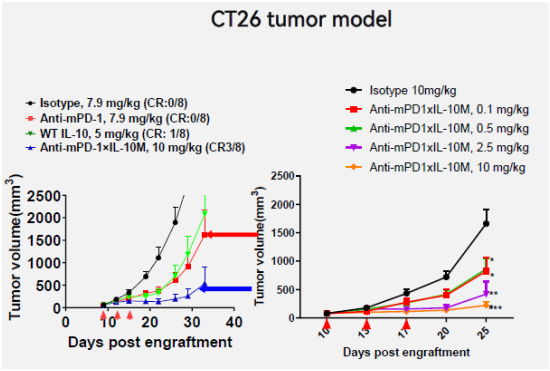
The Status of APD-IL10

An IND application for APD-IL10 is expected to be submitted to the FDA in early 2025.



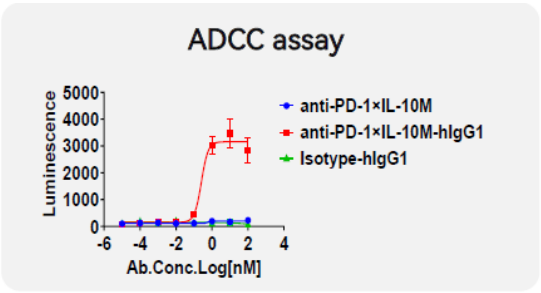
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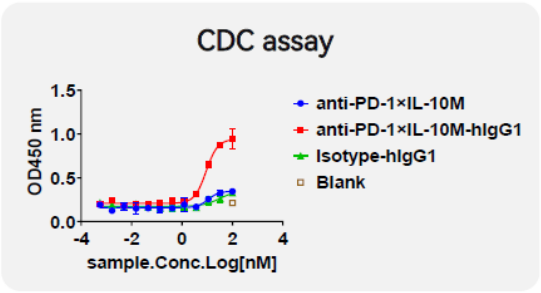
Data



Anti-PD-1xIL-10M vs PD1 Mono-Antibody (*In Vivo*)

APD-IL10 showed stronger anti-tumor efficacy than anti-mPD-1 in CT26 tumor model.





Safety of Anti-PD-1xIL-10M (*In Vitro*)

APD-IL10 had no ADCC and CDC activity, and the risk of cytokine storm was low *in vitro*.

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