Therapeutic Bispecific Antibody for Solid Tumors

Targeting PD-1 and Siglec-15

Overview

Drug Name	PBI-108
Description	PBI-108, a humanized bispecific antibody targeting PD-1 and Siglec-15, regulates tumor killing function of immune cells in the tumor microenvironment. The candidate is in preclinical development.
Target	PD-1 and Siglec-15
Drug Modality	Bispecific antibody
Indication	Solid tumors
Product Category	Immunotherapy
Mechanism of Action	Specifically binding PD-1 and siglece-15 to regulate the tumor killing function of immune cells
Status	Preclinical
Patent	Granted

Collaboration Opportunity

Protheragen Inc. is actively seeking partnership for PBI-108. Potential collaboration can be strategic alliance, licensing, or marketing agreement.
We look forward to hearing from you.

Target

Programmed Cell Death 1 (PD-1)

Introduction	PD-1 is a membrane protein of the immunoglobulin superfamily and is composed of 288 amino acids. PD-1 is expressed on T cells, pro-B cells, and myeloid-derived

	dendritic cells, leading to negative regulation of proliferation and activity of these cells. PD-1 on immune cells engages with programmed death ligand 1 (PD-L1) on cancer cells to facilitate cancer immune escape.
Approved Name	Programmed cell death 1
Official Symbol	PDCD1
Gene Type	Gene with protein product
Synonyms	CD279; PD1; hSLE1; PD-1
Ensembl	ENSG00000188389
Gene ID	5133
mRNA Refseq	NM_005018
Protein Refseq	NP_005009
OMIM	600244
UniProt ID	Q15116
Chromosome Location	2q37.3

Sialic Acid-binding Immunoglobulin-like Lectin 15 (Siglec-15)

Introduction	Siglecs-15, also known as CD33L3, is a specific member of the Siglecs family. Siglecs family are cell surface proteins that play an important role in regulating immune homeostasis. Siglec-15 is a type I transmembrane protein with an extracellular domain consisting of two immunoglobulin-like domains, a transmembrane domain containing lysine residues, and a cytoplasmic tail. Siglece-15 plays an important role in osteolysis and remodeling, microbial infection, and tumor processes.
Approved Name	Sialic acid binding Ig like lectin 15
Official Symbol	SIGLEC15
Gene Type	Gene with protein product
Synonyms	Siglecs-15; HsT1361; CD33L3
Ensembl	ENSG00000197046
Gene ID	284266
mRNA Refseq	NM_213602
Protein Refseq	NP_998767
OMIM	618105
UniProt ID	Q6ZMC9
Chromosome Location	18q21.1

Drug Modality

Bispecific Antibody

PBI-108 is a humanized bispecific antibody that specifically binds to Siglec-15 and PD-1 with high affinity and blocking activity. PBI-108 has a unique format and showed a half-life of 3 days in transgenic mice expressing human neonatal Fc receptor (hFcRn).

Indication

Solid Tumors

Solid tumors are abnormal masses of tissue that usually do not contain cysts or areas of fluid. Solid tumors may be benign or malignant. Different types of solid tumors are named for the cell type that forms them, such as sarcomas, carcinomas, and lymphomas. There were an estimated 18.1 million cancer cases worldwide in 2020. Of these, 9.3 million cases were in men and 8.8 million in women. Cancer is the leading cause of death worldwide, accounting for nearly 10 million deaths in 2020. The most common cancers and most common causes of cancer death in 2020 were all solid tumors, including breast, lung, colon and rectum, and stomach cancers.

Cancer treatment usually includes surgery, radiotherapy, chemotherapy, hormonal treatments, and targeted biological therapies. Cancer treatment decisions should take into account the stage and biology of the tumor, risk and prognosis of planned therapy, and the economic costs associated with therapy. The global solid tumor cancer treatment market was estimated at $121.3 billion in 2018 and is projected to reach $424.6 billion by 2027, increasing to CAGR by 15.0% from 2019 to 2027.

Mechanism of Action

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Regulating the Tumor Killing Function of Immune Cells

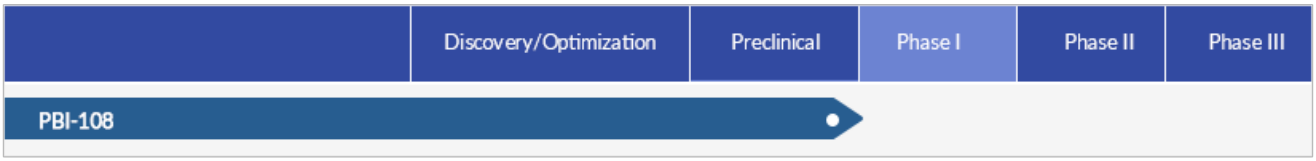
In the tumor microenvironment, the activation of PD-1/PD-L1 pathway suppresses the anti-tumor immune response of effector T cells. Therapies that block this pathway can effectively improve antitumor immune responses against multiple tumor types. Blocking the PD-1/PD-L1 pathway alone may trigger local tumor immune remodeling and restore anti-tumor effects, which causes the majority of patients to show primary or acquired resistance to anti-PD-1 /PD-L1 therapy.

Siglec-15 is expressed on different types of cancer cells including colon cancer, endometrioid carcinoma, thyroid cancer, bladder cancer, kidney cancer, lung cancer, and liver cancer. Siglec-15 suppresses T cell proliferation and cytokine production by engaging unknown receptors. IL-10 is a regulator of the inhibitory function of Siglec-15. In addition, Siglec-15 may also act as a receptor on macrophages to produce TGF-β after binding to sialic acid ligand Sialyl-Tn on tumor cells. The increased levels of IL-10 and TGF-β in the microenvironment will further amplify the immunosuppressive effect of Siglec-15.

The expression of Siglec-15 and PD-L1 is mutually exclusive, implying that anti-Siglec-15 may be a powerful supplement to anti-PD-1/PD-L1. By targeting PD-1 and Siglec-15, PBI-108 can reverse immunosuppression and promote anti-tumor immune responses of immune cells in tumor microenvironment.

Status

The Status of PBI-108



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