BIEH-ab for the Treatment of Non-Small Cell Lung Cancer

Overview

Drug Name	BIEH-ab
Description	BIEH-ab, a bispecific antibody targeting epidermal growth factor receptor and hepatocyte growth factor receptor, is in early clinical development for the treatment of solid tumors, including non-small cell lung cancer.
Target	EGFR; HGFR
Drug Modality	Antibody
Indication	Non-Small Cell Lung Cancer
Product Category	Cancer Immunotherapy
Mechanism of Action	Signal Transduction Modulators
Status	Phase I
Patent	Granted

Seeking Global Cooperation

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

Target

Epidermal Growth Factor Receptor (EGFR)

The epidermal growth factor receptor (EGFR), a commonly expressed transmembrane glycoprotein of the growth factor receptor tyrosine kinase family, was one of the first receptors found to be encoded by proto-oncogenes. It is expressed in many normal human tissues and activation of the proto-oncogene results in elevated expression of the receptor in many types of human tumors. The extracellular domain of the EGFR

binds several ligands, including EGF and transforming growth factor alpha (TGF-alpha). Ligand binding activates the tyrosine kinase activity of the intracellular domain of the EGFR, triggering mechanisms leading to cell division and proliferation, tumor cell dissemination, and escape from apoptosis. In general, tumor cells require smaller amounts of exogenously supplied growth factors to proliferate than normal cells. This may, in part, be due to their ability to respond to endogenously produced growth factors, such as TGF-alpha. In addition, overexpression of growth factor receptors, such as EGFR, is seen in a variety of tumors and allows the tumor to respond to low concentrations of growth factors. EGFR and its ligands are overexpressed in a number of solid tumors including lung cancer. The relationship between EGFR and clinically aggressive malignant disease makes this receptor a promising target for lung cancer therapy.

Hepatocyte Growth Factor Receptor (cMET)

This gene encodes a member of the receptor tyrosine kinase family of proteins and the product of the proto-oncogene MET. The encoded preproprotein is proteolytically processed to generate alpha and beta subunits that are linked via disulfide bonds to form the mature receptor. Further processing of the beta subunit results in the formation of the M10 peptide, which has been shown to reduce lung fibrosis. Binding of its ligand, hepatocyte growth factor, induces dimerization and activation of the receptor, which plays a role in cellular survival, embryogenesis, and cellular migration and invasion. Mutations in this gene are associated with papillary renal cell carcinoma, hepatocellular carcinoma, and various head and neck cancers. Amplification and overexpression of this gene are also associated with multiple human cancers.

Indication

Non-Small Cell Lung Cancer (NSCLC)

Lung cancer is the most prevalent and costly malignancy in the world today, as well as the most frequent cause of cancer-related mortality in both men and women worldwide. According to the International Agency for Research on Cancer (IARC), lung cancer is the malignancy of the highest impact in the world nowadays, both in terms of the total number of individuals it affects (2.1 million new cases in 2018, representing 11.6% of all

new cancer patients) and the total number of resulting deaths (1.76 million in 2018, which is 18.4% of all cancer deaths). The two most common forms of lung cancer are non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC).

NSCLC is further subdivided according to the type of cell in which cancer develops into squamous cell carcinoma, adenocarcinoma, lung adenocarcinoma and large cell carcinoma, as well as more poorly differentiated variants. NSCLC, the more common form of lung cancer, typically grows and spreads slowly. In contrast, SCLC is more aggressive, lethal and metastatic, being characterized by rapid tumor growth, high vascularity, genomic instability and early and frequent metastatic dissemination, as well as a high rate of autoimmune paraneoplastic syndromes and increased risk of developing a second primary tumor.

Mechanism of Action

Signal Transduction Modulators

Molecular Mechanism	Targeting both epidermal growth factor receptor (EGFR) and hepatocyte growth factor receptor (cMET)

Status

The Status of BIEH-ab

The international patent applications under the PCT have been granted.

	Discovery/Optimization	Preclinical	Clinical
BIEH-ab			

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