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Eisai Co., Ltd.
PRISM BioLab Co., Ltd.

The CREB-binding protein (CBP)/β-catenin inhibitor E7386, co-created by Eisai and PRISM BioLab, achieved the clinical POC (Proof of Concept)

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and PRISM BioLab Co., Ltd. (Headquarters: Kanagawa, President and CEO: Dai Takehara, "PRISM") announced today that the CREB-binding protein (CBP) / β-catenin inhibitor E7386, a medium-molecular weight compound created through collaboration research between Eisai and PRISM, has achieved the clinical POC (Proof of Concept).

Eisai is conducting a Phase I clinical study of E7386 monotherapy for solid tumors, and a Phase Ib clinical trial of E7386 plus lenvatinib mesylate (product name: LENVIMA®, "lenvatinib"), the orally available multiple receptor tyrosine kinase inhibitor discovered by Eisai, for solid tumors including hepatocellular carcinoma. The achievement of the POC, which is defined in a collaborative research agreement between Eisai and PRISM, was confirmed based on data such as antitumor activity and changes of biomarkers in these clinical trials.

The E7386 targets, β-catenin, is considered to be one of the undruggable targets that are particularly difficult to develop into drug discovery. β-catenin, along with CBP, which is also the target of E7386, is located at the downstream of the Wnt signaling and regulates the Wnt signaling-dependent transcription activity. E7386 is a CBP / β-catenin inhibitor that inhibits CBP and β-catenin protein-protein interactions and regulates the Wnt signal-dependent gene expression. It is expected to suppress tumor growth dependent on the Wnt signaling. [1] E7386 is also expected to release the suppression of tumor-infiltrating T cells by the Wnt signaling activation, and to enhance the effect of immune checkpoint inhibitors[1]. The antitumor effect of E7386 alone and the combination of E7386 and anti-PD-1 antibody has been confirmed in a cancer-bearing mouse model. [1]

Based on the POC achievement, Eisai has initiated a phase Ib/II clinical trial (Study 201) of E7386 in combination with anti-PD-1 therapy pembrolizumab for solid tumors in Japan.*

Dr. Takashi Owa, Senior Vice President, President of Oncology Business Group, at Eisai said, "With achieving the POC, we are confident with the prospect of offering E7386 to patients as a cancer treatment. E7386 may overcome lenvatinib and pembrolizumab treatment resistances through its combination therapy with lenvatinib or pembrolizumab. Eisai will accelerate clinical trials of E7386 in combination with lenvatinib or pembrolizumab, and do its utmost aiming to create new treatments for cancers with high unmet medical needs."

Dai Takehara, President and CEO of PRISM commented, "The approval of the clinical POC for the E7386 demonstrates that PRISM's drug discovery platform is an effective option for novel drug targets which have been considered difficult. We are grateful to Eisai for advancing this development. We will continue to take on the challenge of targeting more novel targets, with the aim of providing new treatment to as many patients as possible."

* Study 201 is being conducted under a clinical trial collaboration and supply agreement between Eisai and Merck & Co., Inc., Kenilworth, N.J., U.S.A.

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[Notes to editors]

1. About Eisai

Eisai is a leading global research and development-based pharmaceutical company headquartered in Japan, with approximately 10,000 employees worldwide. We define our corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our human health care (*hhc*) philosophy. We strive to realize our *hhc* philosophy by delivering innovative products in therapeutic areas with high unmet medical needs, including Oncology and Neurology.

In the spirit of *hhc*, we take that commitment even further by applying our scientific expertise, clinical capabilities and patient insights to discover and develop innovative solutions that help address society's toughest unmet needs, including neglected tropical diseases and the Sustainable Development Goals.

For further information on Eisai Co., Ltd., please visit https://www.eisai.com and connect with us on Twitter @Eisai_SDGs.

2. About PRISM BioLab

PRISM BioLab Co., Ltd., is a biotechnology company with proprietary small molecule drug discovery platform "PepMetics™ Technology". The PepMetics™ Molecules are designed to mimic α-helix or β-turn peptide using a unique stable scaffold with corresponding dihedral angles. These motifs are essential for protein-protein interactions within the cell, especially related to transcription and translation. Using our small molecule drug discovery technology, two clinical-stage assets for cancer and fibrosis have been developed and licensed. Further, PRISM is working on new drug targets in collaboration with Global and Japanese pharmaceutical companies.

3. About Wnt

Wnt is a glycoprotein with a molecular weight of about 40,000, which is conserved across organisms from nematodes and Drosophila to mammals, and it is reported to control early development, morphogenesis, organogenesis, and cell proliferation, differentiation, and motility after birth. Pathways known to comprise the Wnt signaling pathway include the Wnt / β-catenin pathway which is associated with cell differentiation and dorsal formation, the Wnt / PCP pathway which is involved in planar cell polarity and motility during gastrulation, the Wnt / Ca^{2+} pathway which plays a role in embryonic isolation and the pathway involved in the regulation of muscle regeneration. The most well-known Wnt signaling is the Wnt / β-catenin pathway. It has been reported that β-catenin induces gene expression as a mediator of Wnt signaling, and as a result regulates cell proliferation and differentiation. β-catenin, along with RAS, P53 and MYC, is called "Cancer's Big 4" and is considered to be one of the undruggable targets that are difficult to develop into drug discovery.

4. About E7386

E7386 is a CBP / β-catenin inhibitor that inhibits protein-protein interactions between the transcription coactivator CBP and β-catenin, and regulates the Wnt signaling-dependent gene expression. Since E7386 acts on the CBP / β-catenin transcription complex located at the most downstream of the Wnt signaling, it is expected to inhibit not only ligand-dependent activation but also activation caused by gene mutations in Wnt signaling factors such as adenomatous polyposis coli (APC) and β-catenin.

[1]Cancer Res. 2021 Feb 15;81(4):1052-1062.
https://cancerres.aacrjournals.org/content/81/4/1052.full-text.pdf