

EISAI ENTERS INTO COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT WITH PRISM BIOLAB CONCERNING CBP/ β -CATENIN INHIBITING COMPOUNDS

Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito, "Eisai") announced today that it has entered into a license and collaborative research and development agreement with PRISM BioLab Corporation (Headquarters: Yokohama, President & CEO: Hiroyuki Kouji, "PRISM") concerning a CBP/ β -catenin inhibitor ("the Compound") and analogous compounds thereof.

Under the terms of the agreement, PRISM shall grant Eisai the following rights: 1) the exclusive worldwide rights (excluding some countries) to develop and commercialize the Compound as well as pharmaceutical products that contain the Compound as an active ingredient for the treatment of solid tumors and leukemia, with the right to sublicense; 2) the option to acquire the exclusive worldwide rights (excluding some countries) to develop and commercialize analogous compounds of the CBP/ β -catenin inhibitor and pharmaceutical products that contain analogous compounds as an active ingredient for the treatment of solid tumors and leukemia, with the right to sublicense.

The Compound, a small molecule that inhibits CBP/ β -catenin complex formation, was discovered using PRISM's proprietary intracellular protein-protein interaction inhibitor/modulator library. Phase Ia/Ib clinical trials of the Compound were initiated in the United States in March of this year¹⁾.

In accordance with advancements in genetic science, scientists have identified proteins that are related to the growth of cancer cells. Against this backdrop, much research is currently being conducted to investigate the involvement of the Wnt signaling pathway in cancer onset and progression. CBP (CREB (cyclic AMP Response Element binding protein) binding protein) is a transcription cofactor that binds to β -catenin, a transcription factor activated by extracellular stimulation. Homeostatic activation of the Wnt/ β -catenin signaling pathway triggers cancer onset, with these mutated pathway proteins often found in cancer cells. This has led investigators to study the use of substances that inhibit this pathway as potential novel anticancer agents, with small molecules and biological agents reportedly having demonstrated inhibitory activity thus far^{2), 3)}.

Eisai defines oncology as a therapeutic area of focus and is committed to the development of novel anticancer agents and treatments for supportive care. With the conclusion of this agreement, Eisai seeks to make further contributions to address the diversified needs of and increase benefits provided to cancer patients and their families as well as healthcare professionals.

[Please refer to the following notes on PRISM BioLab Corporation, Wnt, β -catenin, and Wnt signaling pathway, and overview of Eisai oncology]

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[Notes to editors]

1. About PRISM BioLab Corporation

PRISM BioLab Corporation, established in 2006 and headquartered in Yokohama, is a bioventure company focused on the development of novel therapeutic compounds using a unique small molecule platform technology that is capable of regulating protein-protein interaction.

2. About Wnt

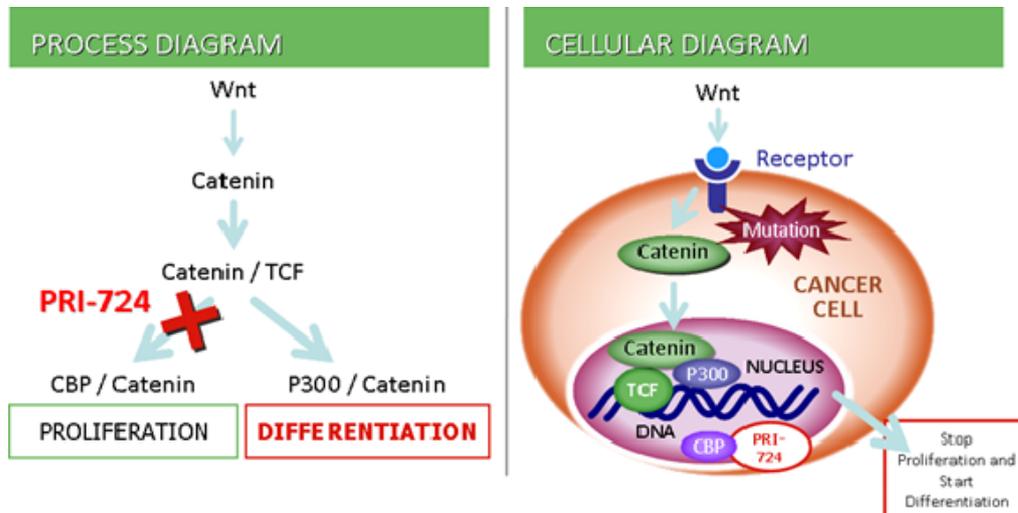
Wnt is a glycoprotein that plays a central role in axis formation, central neurogenesis and organogenesis. The name Wnt was coined due to the protein's shared homology with the wingless gene which was originally identified as a mutation of Mouse Mammary Tumor Virus infected breast cancer causing genes and involvement in segment formation of drosophila (fruit fly). 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/Ca²⁺ pathway which plays a role in embryonic isolation, and the pathway involved in the regulation of muscle regeneration.

3. About β -Catenin

Catenin is a cytoskeletal-associated protein that is known to come in several subtypes (α , β , and γ). β -catenin not only plays an important role in catenin-mediated cell binding and cytoskeletal formation, it is also involved in gene expression regulation as a component of the Wnt signaling pathway. While the amount of β -catenin expressed in normal cells is regulated, the impairment of regulation mechanisms in various cancer cells is known to lead to an increased amount of intracellular β -catenin, which is characteristic of tumor tissue⁴.

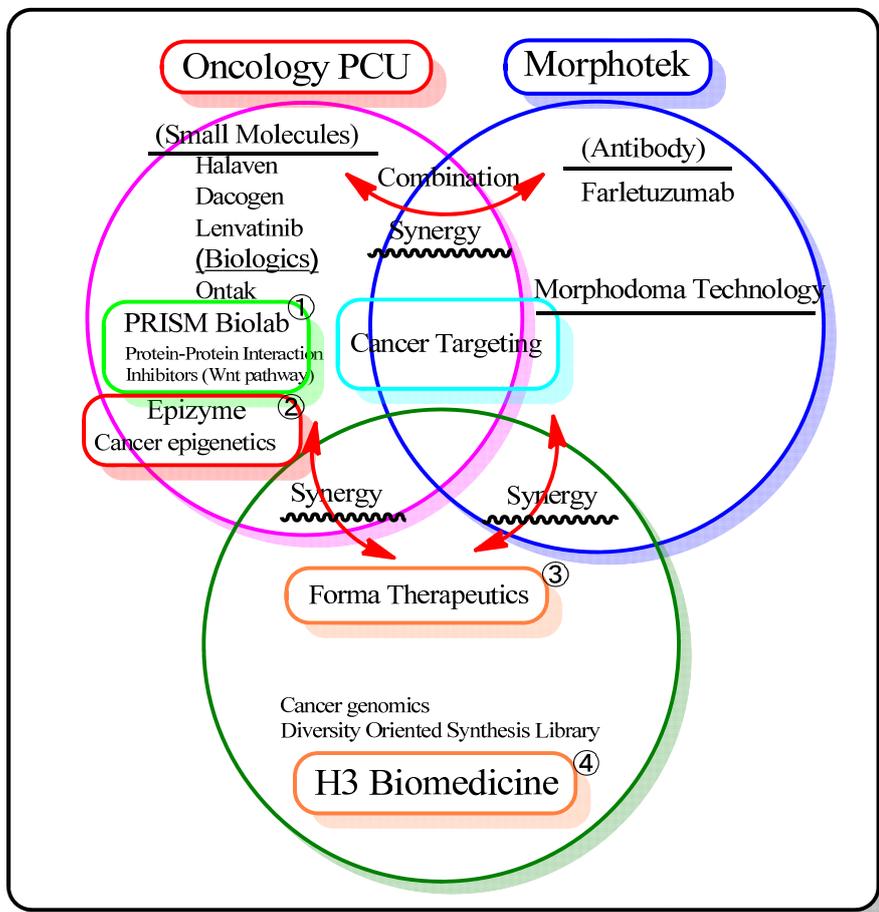
4. Wnt Signaling Pathway Diagram

The following diagrams illustrate how the above-mentioned factors mutually interact with each other. (PRI-724 is one of CBP/ β -catenin inhibitor)



5. Overview of Eisai Oncology

Eisai oncology consists of 1) Oncology PCU (Product Creation Unit), 2) Morphotek, Inc. and 3) H3 Biomedicine Inc. The relationship and research focuses of these functions are shown below.



① PRISM Biolab: Alliance in April 2011, ② Epizyme: Alliance in March 2011, ③ Forma Therapeutics: Alliance in November 2010, ④ H3 Biomedicine: Established in January 2011.

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- 1) Safety and Efficacy Study of PRI-724 in Subjects With Advanced Tumors (<http://clinicaltrials.gov/ct2/show/NCT01302405?term=PRI-724&rank=1>)
 - 2) http://www.funakoshi.co.jp/news/100315spdf/100315s_p10.pdf
 - 3) Shih-Min A. Huang et al, Tankyrase inhibition stabilizes axin and antagonizes Wnt signalling. Nature, Vol 461, 1 October 2009. doi:10.1038/nature08356
 - 4) Chie Sakanaka, Innovation in Wnt Research, Jikken Igaku, Vol 26, (3)391, 2008