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Eisai Co., Ltd.

EISAI SUBMITS MARKETING AUTHORIZATION APPLICATION IN JAPAN FOR ANTICANCER AGENT TAZEMETOSTAT FOR EZH2 GENE MUTATION-POSITIVE FOLLICULAR LYMPHOMA

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has submitted a marketing authorization application in Japan for the EZH2 inhibitor tazemetostat hydrobromide (generic name, development code: E7438, "tazemetostat") for EZH2 gene mutation-positive follicular lymphoma.

This application is based on the results of a multicenter, open-label, single-arm clinical phase II trial (Study 206) in Japan conducted by Eisai and other studies conducted by Epizyme, Inc. (Headquarters: Massachusetts, United States) outside Japan. Study 206 enrolled patients with EZH2 gene mutation-positive, primarily follicular lymphoma which had relapsed or was refractory. The primary endpoint of this study was objective response rate, and secondary endpoints included safety. Detailed results of the study will be presented at upcoming academic conferences.

Tazemetostat is a first-in-class, oral EZH2 inhibitor discovered by Epizyme, Inc. This agent is known to selectively inhibit EZH2, an epigenetic enzyme which belongs to the histone methyltransferase family and may have an important role in carcinogenesis. This results in the control of expression of various cancer-related genes, leading to the suppression of proliferation of cancer cells. Eisai is responsible for development and commercialization of tazemetostat in Japan, while Epizyme, Inc. is responsible for all regions outside Japan. In June, tazemetostat received accelerated approval for follicular lymphoma in the United States.

Follicular lymphoma is a low-grade B-cell lymphoma that accounts for 10-20% of non-Hodgkin's lymphomas. Follicular lymphoma is generally slow-growing and sensitive to chemotherapy. However, development of a new treatment strategy is required for follicular lymphoma which still remains difficult to cure, as recurrence often occurs repeatedly. Since 7% to 27% of follicular lymphomas are reported to have gain-of-function mutations in the EZH2 gene, it is estimated that there are approximately 600 to 2400 patients with follicular lymphoma with EZH2 mutations in Japan.

Eisai positions oncology as a key franchise area and aims to create innovative drugs that act towards *curing cancer*. Eisai will continue to create innovation in the development of new drugs based on cutting-edge cancer research, and aims to make continuous efforts to meet the diversified needs of and increase the benefits provided to patients with cancer, their families, and healthcare professionals.

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[Notes to editors]

1. About epigenetics

Epigenetics is a branch of science that studies the mechanism for the acquired activation/inactivation of gene function and seeks to determine how gene function is inherited through cell division, irrespective of DNA base sequence alteration. Examples of modification that lead to the regulation of gene expression include methylation of DNA and modifications of histone (methylation, acetylation, phosphorylation, etc.).

2. About EZH2

EZH2 is one of the histone methyltransferases within a larger class of epigenetics-related proteins, and specifically catalyzes the methylation of histone H3 at lysine 27 (H3K27), thus controlling expression of various genes. It is indicated that an increase in methylation of H3K27 caused by EZH2 gain-of-function mutation, overexpression, or the dysfunction of EZH2 suppressive factors plays an important role in carcinogenesis.

3. About Tazemetostat (Development Code: E7438, Epizyme, Inc.'s Development Code: EPZ-6438)

Created through Epizyme's proprietary product platform, tazemetostat is a first-in-class small molecule inhibitor of the epigenetic enzyme EZH2. This agent selectively inhibits EZH2 in a competitive matter with S-adenosylmethionine (a methyl group donor) to suppress methylation of H3K27. In the United States, it received accelerated approval in January 2020 for the treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma who are not eligible for complete resection. Additionally, in June 2020 it received accelerated approval for two distinct follicular lymphoma (FL) indications: 1) adult patients with relapsed or refractory FL whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least two prior systemic therapies, and 2) adult patients with relapsed or refractory FL who have no satisfactory alternative treatment options.