No.21-08

February 22, 2021
Eisai Co., Ltd.

MHLW GRANTS ORPHAN DRUG DESIGNATION IN JAPAN TO NOVEL FIBROBLAST GROWTH FACTOR (FGF) RECEPTOR SELECTIVE TYROSINE KINASE INHIBITOR E7090 WITH PROSPECTIVE INDICATION FOR UNRESECTABLE BILIARY TRACT CANCER WITH *FGFR2* GENE FUSION

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has received orphan drug designation for a prospective indication for unresectable biliary tract cancer with *FGFR2* gene fusion by the Ministry of Health, Labour and Welfare, Japan (MHLW) for its in-house discovered fibroblast growth factor (FGF) receptor (FGFR1, FGFR2, FGFR3) selective tyrosine kinase inhibitor E7090, which is currently under development as an orally available novel anti-cancer agent.

FGFRs with genetic aberrations are known to play an important role in the proliferation, survival and migration of cancer cells as well as tumor angiogenesis and drug resistance. These genetic aberrations in FGFRs have been observed in various types of cancers, therefore, there is growing interest in FGFRs as a promising target for cancer therapy. By selectively inhibiting FGFR1, 2 and 3, and blocking those signals, E7090 has the potential to become a new molecular targeted therapy for cancers with FGFR genetic aberrations.
In Japan, a Phase I clinical trial of E7090 was conducted, and E7090 has been designated as the target drug for the SAKIGAKE Designation System of the MHLW for the treatment of unresectable biliary tract cancer. Currently, a Phase II clinical trial (Study 201) of E7090 is underway in patients with cholangiocarcinoma with *FGFR2* gene fusion in Japan and China.

Eisai positions oncology as a key therapeutic area and is aiming to discover innovative new medicines with the potential to cure cancer. Eisai is committed to exploring the potential clinical benefits of E7090 for cancer treatment, as it seeks to contribute further to addressing the diverse needs of, and increasing the benefits provided to, patients with cancer and their families.

Media Inquiries:
Public Relations Department,
Eisai Co., Ltd.
+81-(0)3-3817-5120

[Notes to editors]

1. About E7090

Discovered in-house by Eisai's Tsukuba Research Laboratories, E7090 is an orally available novel tyrosine kinase inhibitor that demonstrates selective inhibitory activity against fibroblast growth factor receptors (FGFR) FGFR1, FGFR2 and FGFR3. Distinct from prior known FGFR inhibitors, E7090 has a basic structure which lacks the dimethoxyphenyl moiety, and in a kinetic interaction analysis study, it was observed that E7090 demonstrates antitumor effects due to inhibition of kinase activity with a binding mode (Type V) that exhibits rapid and potent binding as well as high selectivity to FGFR.[1]

A Phase II clinical trial (Study 201) of E7090 is underway in Japan and China to evaluate efficacy and safety in patients with cholangiocarcinoma with *FGFR2* gene fusion. A Phase I clinical trial of E7090 is also underway in Japan in patients with estrogen receptor-positive and HER2-negative breast cancer.

2. About Biliary Tract Cancer with *FGFR2* Gene Fusion

The five-year survival rate for biliary tract cancer is approximately 20%, which makes it an intractable cancer with the second worst prognosis following pancreatic cancer.[2] Drug therapy options are limited in comparison with other cancers, and as such it is a disease with significant unmet medical needs. The estimated number of patients with biliary tract cancer is approximately 32,000 in Japan.[3,4,5] *FGFR2* gene fusion is observed in approximately 14% of intrahepatic cholangiocarcinoma, which account for 15-30% of biliary tract cancers.[6]

3. Orphan Drug Designation System in Japan

The orphan drug designation system in Japan aims to support the development of drugs for diseases for which the number of patients is small and research and development is not progressing, despite high unmet medical need. As the requirement for designation based on Article 77-2 of the Pharmaceutical and Medical Device Act (PMD Act) of Japan, a drug must meet the following conditions in order to be considered for orphan drug designation in Japan: the number of people expected to use the drug for its intended use is less than 50,000 people in Japan; there is no suitable alternative drug or treatments in Japan, or the proposed drug is expected to be significantly more effective or safer than drugs already available on the Japanese market; and there is a scientific rationale to support the necessity of the drug for the target disease, and the development plan for the drug is appropriate. Specific measures to support the development of orphan drugs include giving prioritized consultation regarding clinical development and conducting priority examinations, reducing application fees, extending registration validity period, granting subsidies for research and development expenditures, and tax incentives.

[1] Watanabe Miyano S. et al., "E7090, a Novel Selective Inhibitor of Fibroblast Growth Factor Receptors, Displays Potent Antitumor Activity and Prolongs Survival in Preclinical Models", *Molecular Cancer Therapeutics,* 2016, 15(11), 2630-2639.

[2] Latest statistics, Cancer Information Service, National Cancer Center, Japan.

[3] Official Statics of Japan (e-Stat), 2017 Patient Survey https://www.e-stat.go.jp/

[4] The 21st Follow-up Survey Reports for Primary Liver Cancer Cases in Japan (2010-2011), 2020.

[5] Shin Ishihara. et al., "Biliary tract cancer registry in Japan from 2008 to 2013", *J Hepatobiliary Pancreat Sci.,* 2016, 23, 149-157.

[6] Arai Y. et al., "Fibroblast growth factor receptor 2 tyrosine kinase fusions define a unique molecular subtype of cholangiocarcinoma", *Hepatology*, 2014, 59, 1427-1434.