No.17-51

September 22, 2017
Eisai Co., Ltd.

EISAI PRESENTS LATEST NON-CLINICAL DATA ON ITS FIRST ANTIBODY-DRUG CONJUGATE MORAB-202 AT 8th ANNUAL WORLD ADC

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that the latest non-clinical data on MORAb-202, Eisai's first antibody-drug conjugate (ADC) developed by its research subsidiary Morphotek, Inc., was presented at the 8th Annual World ADC.[1-2]

MORAb-202 is a new ADC which combines farletuzumab, an investigational anti-folate receptor alpha (FRA) antibody, with a payload* of Eisai's in-house developed anticancer agent eribulin (generic name: eribulin mesylate, product name: Halaven®).

The presentation at the 8th Annual World ADC covered the results of non-clinical studies investigating MORAb-202. MORAb-202 demonstrated high selectivity for FRA-positive cancer cells, which are expressed in approximately 60% of triple-negative breast cancer patients, as well as strong antitumor activity. Furthermore, there was a confirmed bystander effect**, with MORAb-202 also exhibiting antitumor activity on the FRA-negative cancer cells surrounding the FRA-positive cancer cells. MORAb-202 showed high selectivity for FRA-positive cancer cells and a long half-life in the blood (111-178 hours), and in mouse models inoculated with cancer, a 60-day tumor regression effect was observed based a single dose using only a fifth of eribulin's clinical dosage.

After MORAb-202 enters the target cancer cells, the linker is enzymatically cleaved, separating eribulin, the payload, from the antibody. The released eribulin then displays its original high antitumor effects. Additionally, ADCs have been known to have high aggregation levels due to the influence of hydrophobic payloads, but since MORAb-202 employs the water-soluble eribulin as a payload, aggregation is under 1%. Due to this characteristic of reaching the cancer cells without aggregating in the blood, MORAb-202 suggests a high safety profile.
With its base of Eisai's in-house developed eribulin, MORAb-202 demonstrates new generation ADC characteristics, namely, internalization into target cancer cells, an antitumor effect followed by a bystander effect after its releasing its drug payload, and aggregation inhibition.
Eisai plans to move MORAb-202 into the clinical stage during the latter half of FY 2017.

Eisai positions oncology as a key therapeutic area, and is aiming to discover revolutionary new medicines with the potential to cure cancer. The company will continue to create innovation in the development of new drugs based on cutting-edge cancer research, as it seeks to contribute further to addressing the diverse needs of, and increasing the benefits provided to, patients with cancer, their families, and healthcare providers.

* Payload: An anticancer agent connected to an antibody via a linker in an ADC.
** Bystander effect: When the anticancer agent and antibody parts of an ADC are separated inside a targeted antigen-positive cancer cell, the released anticancer agent also affects neighboring antigen-negative cancer cells and the component cells of the cancer microenvironment.

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[Notes to editors]

1. About Morphotek, Inc. and MORAb-202

Morphotek, Inc., a subsidiary of Eisai Inc.in the United States, is a biopharmaceutical company specializing in the development of protein and antibody products through the use of a novel and proprietary gene evolution technology. Morphotek, Inc. developed MORAb-202, which combines anticancer agent farletuzumab, an IgG1 monoclonal antibody that binds to the folate receptor alpha, and Eisai's in-house developed anticancer agent eribulin using an enzyme cleavable linker. After entering the target cancer cells, the linker is enzymatically cleaved, separating eribulin from the antibody, which is thought to create a therapeutic effect on the cancer cells and surrounding cancer microenvironment. Morphotek, Inc. is currently preparing MORAb-202 for Phase I clinical trials.

In non-clinical studies, MORAb-202 demonstrated high target selectivity for FRA-positive cancer cells, strong anticancer activity (50% Inhibitory Concentration (IC_{50}) against FRA-positive cells IC_{50} = 0.001-23nM、FRA-negative cells IC_{50} >100nM), a clear bystander effect in the co-culture of positive and negative FRA-positive cells, long half-life in blood (111-178 hours), and a long-lasting antitumor effect with only a single dose (In mouse models inoculated with triple-negative breast cancer cells and dosed with 5mg/kg, a 60-day tumor regression effect and complete response in 4 out of 8 mice was observed).

Additionally, by leveraging the combination of eribulin, with its unique mechanism of action, in-house developed antibodies, and antibody conjugation technology, Morphotek, Inc. launched a new ADC Services business in April 2017.

2. About farletuzumab (development code: MORAb-003)

Farletuzumab is a humanized, IgG1 monoclonal antibody that binds to the folate receptor alpha (FRA). Farletuzumab is currently undergoing Phase II clinical trials in Japan, the United States and Europe, for the treatment of recurrent platinum-sensitive ovarian cancer with a low CA125 level.

3. About eribulin (generic name: eribulin mesylate, product name: Halaven)

Eribulin is the first in the halichondrin class of microtubule dynamics inhibitors with a novel mechanism of action. Structurally eribulin is a simplified and synthetically produced version of halichondrin B, a natural product isolated from the marine sponge *Halichondria okadai*. Eribulin is believed to work by inhibiting the growth phase of microtubule dynamics which prevents cell division. In addition, recent non-clinical studies showed that eribulin is associated with increased vascular perfusion and permeability in tumor cores. Eribulin promotes the epithelial state and decreases the capacity of breast cancer cells to migrate and invade.

Eribulin was first approved in November 2010 in the United States as a treatment for patients with metastatic breast cancer who have received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting. Eribulin is currently approved for use in the treatment of breast cancer in over 60 countries worldwide, including Japan and countries in Europe, the Americas and Asia. In Japan, eribulin has been approved to treat inoperable or recurrent breast cancer and was launched in the country in July 2011. In addition, eribulin has been approved in countries in Europe and Asia indicated as a treatment for patients with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting, unless patients were not suitable for these treatments.

Regarding soft tissue sarcoma, eribulin was approved in the United States for the treatment of patients with unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen in January 2016, approved in Japan for the treatment of soft tissue sarcoma in February 2016, and approved in Europe for the treatment of adult patients with unresectable liposarcomas who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease in May 2016.

1 Albone E. "MORAb-202 – A Potent Human Folate Receptor Alpha-Targeting ADC that Utilizes the Anti-tubulin Agent Eribulin as Payload" Oral Presentation at the 8th Annual World ADC.

2 Furuuchi K. et al "MORAb-202, a novel antibody-drug conjugates (ADC) comprised of farletuzumab conjugated with eribulin, exhibits long-lasting targeted antitumor activity and payload-mediated bystander effects on the tumor microenvironment." Scientific Poster Session at the 8th Annual World ADC.