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Translation

New Drug Application Filed for Antibody-Drug Conjugate Trastuzumab Emtansine for the Treatment of HER2-Positive Metastatic or Recurrent Breast Cancer

January 29, 2013 (Tokyo) – Chugai Pharmaceutical Co., Ltd. [Main Office: Chuo-ku, Tokyo. Chairman & CEO: Osamu Nagayama (hereafter, "Chugai")] announced today that it has filed a new drug application to the Ministry of Health, Labour and Welfare (MHLW), for antibody-drug conjugate "trastuzumab emtansine (T-DM1)" for the treatment of "HER2-positive metastatic or recurrent breast cancer."

Chugai filed the application with the MHLW based on the results from an overseas phase III clinical trial (the EMILIA trial) and a domestic phase II clinical trial.
The EMILIA trial is an international phase III study comparing T-DM1 alone to lapatinib in combination with capecitabine in people with HER2-positive metastatic or unresectable locally advanced breast cancer who had previously been treated with trastuzumab and a taxane chemotherapy. Japanese patients were not included in the EMILIA trial.

The EMILIA trial had progression free survival (PFS) as one of its primary endpoints, and patients who received T-DM1 experienced a 35 percent reduction in the risk of their disease worsening or death compared to those who received lapatinib plus capecitabine. The median PFS improved by 3.2 months from 6.4 months of lapatinib and capecitabine to 9.6 months of T-DM1 (hazard ratio=0.65; $p<0.0001$).
As for overall survival (OS), another primary endpoint, the results showed the risk of death was reduced by 32% for patients who received T-DM1 compared to those who received lapatinib plus capecitabine. Patients in the study treated with T-DM1 survived a median time of 5.8 months longer than those who received lapatinib and capecitabine (median OS: 30.9 months vs. 25.1 months) (hazard ratio=0.68; $p=0.0006$).
Regarding safety, fewer patients who received T-DM1 experienced Grade 3 or higher AEs than those who received lapatinib plus capecitabine. The most common Grade 3 or higher AEs reported in patients receiving T-DM1, compared to those receiving lapatinib plus capecitabine, included low platelet count and increase of AST and ALT levels.
The phase II trial conducted in Japan confirmed the efficacy and the tolerability of T-DM1 in Japanese patients.

The number of patients newly diagnosed with breast cancer in Japan continues to rise each year and is estimated at approximately 60,000 annual average in 2015-2019*. And HER2 expression has been observed in approximately 20% of breast cancer patients.

As the top pharmaceutical company in the field of oncology, Chugai will work for the approval to provide patients and medical professionals with new treatment options as soon as possible.

* T. Sobue, et al., Cancer White Paper 2012, Shinoharashinsha Inc.

About trastuzumab emtansine (T-DM1)

T-DM1 is comprised of the antibody trastuzumab and the chemotherapy DM1 attached together using a stable linker. T-DM1 is designed to target HER2, inhibit HER2 signalling, induce antibody-dependent cell mediated cytotoxicity, and deliver the chemotherapy DM1 directly inside HER2-positive cancer cells. Once trastuzumab emtansine is taken up by those cancer cells, it is designed to destroy them by releasing the DM1.

A Biologics License Application (BLA) for T-DM1 for people with previously treated, HER2-positive breast cancer has been submitted to the U.S Food and Drug Administration (FDA) by Genentech and a Marketing Authorisation Application has been submitted to the European Medicines Agency (EMA) by Roche. FDA granted priority review for the BLA for T-DM1, with an expected action date of February 26, 2013.

About efforts for making personalised healthcare targeting HER2

Trastuzumab (Herceptin®) is a personalized medicine, developed by Roche, which targets and blocks the function of HER2.

Pertuzumab also targets HER2 but works in a different way to trastuzumab. Pertuzumab is designed specifically to prevent the HER2 receptor from pairing (dimerising) with other types of HER receptors on the surface of cells, a process that is believed to play a role in tumour growth and survival. Binding of pertuzumab to HER2 may also signal the body's immune system to destroy the cancer cells. Chugai filed a new drug application for humanized HER dimerization inhibitory monoclonal antibody pertuzumab on May 25, 2012.

HER2 testing is performed before drug administration in order to determine whether or not a patient is HER2 positive. This allows identification of those patients who are most likely to respond to HER2 targeted treatments. In Japan, HER2 testing has become a common practice, and is performed in about 90% of patients with breast cancer.