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Roche submits application to FDA for trastuzumab-DM1 in previously treated advanced HER2-positive breast cancer

T-DM1 is the first antibody-drug conjugate in Roche's pipeline to be submitted to the FDA

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the company submitted a Biologics Licence Application (BLA) to the U.S. Food and Drug Administration (FDA) for trastuzumab-DM1 (T-DM1) in people with advanced HER2-positive breast cancer who have previously received multiple HER2-targeted medicines and chemotherapies. This submission is based on the results of a Phase II study which showed T-DM1 shrank tumours in one-third of women who had received on average seven prior medicines for advanced HER2-positive breast cancer.

"While we've made great strides in treating HER2-positive breast cancer, there is a group of people whose breast cancer will come back after many treatments, leaving them with very limited options," said Hal Barron, M.D., Global Development and chief medical officer. "Data from studies have shown that T-DM1 shrank tumors in these people, so we are excited to have submitted this application to the FDA in hopes of offering a potential new medicine to people with this type of breast cancer."

T-DM1 is an antibody-drug conjugate (ADC), also known as an armed antibody, being studied for advanced HER2-positive breast cancer. T-DM1 attaches trastuzumab and the chemotherapy DM1 together using a stable linker, which is designed to keep T-DM1 in one piece until it reaches specific cancer cells. The antibody (trastuzumab) binds to the HER2-positive cancer cells, and is thought to block out-of-control signals that make the cancer grow while also calling on the body's immune system to attack the cells. Then, once T-DM1 is absorbed into those cancer cells, it is designed to destroy them by releasing the DM1

About T-DM1 studies

The FDA submission is based on a Phase II study known as TDM4374g, a single-arm, multi-centre trial designed to assess single-agent T-DM1 in 110 women with HER2-positive advanced breast cancer whose disease had worsened after receiving at least two prior HER2-targeted treatments (Herceptin [trastuzumab] and lapatinib) in the metastatic setting, as well as an anthracycline, a taxane and capecitabine. The primary

endpoint of the study was objective response rate (a complete or partial tumor shrinkage of at least 30 percent, determined by two tumor assessments at least 28 days apart), as measured by an independent review facility.

Results from the study were presented at the 2009 San Antonio Breast Cancer Symposium and demonstrated that T-DM1 shrank tumors in 33 percent of women with advanced HER2-positive breast cancer that had worsened following treatment with an average of seven prior medicines for metastatic disease. In the study, most side effects were mild (Grade 1-2) and similar to those observed in previous clinical trials of T-DM1. The most common adverse events of any grade were fatigue (62 percent) and nausea (37 percent). The most common severe adverse events (Grade 3 or higher) were a low level of platelets in the blood (7 percent), fatigue (5 percent) and cellulitis (4 percent). No severe cardiac-specific side effects were observed. One patient with pre-existing, non-alcoholic fatty liver disease died with liver failure. The safety results were consistent with data from earlier studies, including a proof-of-concept Phase II study (TDM4258g), which was also included in the submission to the FDA.

Several Phase II and III trials of T-DM1, either alone or in combination with other medicines, are planned or ongoing:

- An ongoing Phase III trial, known as EMILIA, is comparing T-DM1 to lapatinib in combination with capecitabine in people with advanced HER2-positive breast cancer whose disease has worsened after receiving initial treatment.
- A planned Phase III study, MARIANNE, will compare both T-DM1 alone and T-DM1 in combination with pertuzumab to Herceptin in combination with a taxane chemotherapy in people with advanced HER2-positive breast cancer who have not been previously treated for advanced disease.
- Preliminary results from a Phase II study (TDM4450g) comparing T-DM1 to Herceptin in combination with docetaxel chemotherapy in people with advanced HER2-positive breast cancer who have not been previously treated for advanced disease have been submitted for presentation at a future medical meeting.
- Roche has also opened a T-DM1 Patient Access Study in the United States to provide a specific group of people with advanced HER2-positive breast cancer access to T-DM1 while Roche seeks U.S. approval.

Roche licenses technology for T-DM1 under an agreement with ImmunoGen, Inc. Building on successes

with T-DM1, Roche has approximately 50 ADCs in early stages of research and development for multiple tumor types.

About breast cancer

Breast cancer is the most common cancer among women worldwide.ⁱ Each year more than one million new cases of breast cancer are diagnosed worldwide, and nearly 400,000 people will die of the disease annually.ⁱⁱ

In HER2-positive breast cancer, increased quantities of the HER2 protein are present on the surface of the tumour cells. This is known as 'HER2-positivity' and affects approximately 20-25% of women with breast cancer.

About Herceptin

Herceptin is a humanised antibody, designed to target and block the function of HER2, a protein produced by a specific gene with cancer-causing potential. The mode of action of Herceptin is unique in that it activates the body's immune system and suppresses HER2 to target and destroy the tumour. Herceptin has demonstrated unprecedented efficacy in treating both early and advanced (metastatic) HER2-positive breast cancer. Given on its own as monotherapy as well as in combination with or following standard chemotherapy, Herceptin has been shown to improve response rates, disease-free survival and overall survival while maintaining quality of life in women with HER2-positive breast cancer.

Herceptin is marketed in the United States by Genentech, in Japan by Chugai and internationally by Roche. Since 1998, Herceptin has been used to treat more than 740,000 patients with HER2-positive breast cancer worldwide.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2009, Roche had over 80'000 employees worldwide and invested almost 10 billion Swiss francs in R&D. The Group posted sales of 49.1 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: www.roche.com.

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Roche Group Media Relations

Phone: +41 -61 688 8888 / e-mail: basel.mediaoffice@roche.com

- Alexander Klauser (Head)
- Martina Rupp
- Claudia Schmitt

i World Health Organization, <http://www.who.int/cancer/detection/breastcancer/en/>

ii Ferlay J, et al., GLOBOCAN 2002. Cancer Incidence, Mortality and Prevalence Worldwide. IARC CancerBase No.5, Version 2.0. IARCPress, Lyon, 2004. 2004