

Basel, 19 December 2014

## **Roche provides update on Phase III MARIANNE study in people with previously untreated advanced HER2-positive breast cancer**

- **MARIANNE was designed to evaluate three HER2-targeted regimens in previously untreated (first line) advanced HER2-positive breast cancer (Kadcyla alone, Kadcyla plus Perjeta, Herceptin plus chemotherapy)**
- **Study met non-inferiority endpoint, showing similar progression-free survival (PFS) among the three arms**
- **Study did not meet PFS superiority endpoint for Kadcyla-containing regimens**
- **Results do not impact approved uses of Kadcyla or Perjeta in advanced HER2-positive breast cancer**

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today top-line results of the Phase III MARIANNE study. The study evaluated three HER2-targeted regimens – Kadcyla® (trastuzumab emtansine) plus Perjeta® (pertuzumab), Kadcyla alone, and Herceptin® (trastuzumab) plus taxane chemotherapy – in people with previously untreated (first line) advanced HER2-positive breast cancer. The study showed the three regimens helped people live without their disease worsening (PFS) for a similar amount of time, meeting its non-inferiority endpoint as assessed by an Independent Review Committee (IRC). However, neither Kadcyla-containing treatment arm significantly improved PFS compared to Herceptin and chemotherapy. Adverse events observed in the two experimental arms of the study were generally consistent with those seen in previous studies of Kadcyla and/or Perjeta<sup>1</sup>.

In their approved uses for advanced HER2-positive breast cancer, Kadcyla and Perjeta have been shown to extend survival. Kadcyla is approved for people with previously treated disease (second and later lines). Perjeta is approved in combination with Herceptin and chemotherapy for people with previously untreated disease (first line).

“Over the past 30 years, we have made significant progress in treating one of the most aggressive forms of advanced breast cancer with medicines that extend patients’ lives across the course of their disease. In this study, we had hoped to show improvement in progression-free survival without the use of traditional chemotherapy in the first line treatment of patients with advanced HER2-positive breast cancer,” said Sandra

Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "While MARIANNE didn't achieve this result, we will continue to study these medicines, as well as investigational treatments for other types of breast cancer, with the goal of improving outcomes for patients."

Data from the MARIANNE study will be presented at an upcoming medical meeting. Roche will discuss the data with health authorities.

### **About the MARIANNE Study**

The Phase III MARIANNE study (NCT01120184; BO22589) is an international, randomized, multicenter, three-arm study involving 1,095 people with HER2-positive advanced breast cancer – either with inoperable locally advanced disease that had worsened during or returned after previous treatment, or with disease that had spread to other areas of the body.<sup>2</sup> People with advanced breast cancer at diagnosis and people whose disease had worsened following either neoadjuvant or adjuvant treatment were eligible.

People enrolled in the study received treatment with either:

- A combination of Kadcyła and Perjeta
- Kadcyła alone, or
- Herceptin and either docetaxel or paclitaxel chemotherapy.

The primary endpoint of the MARIANNE study is PFS as assessed by an Independent Review Committee (IRC). Secondary endpoints include overall survival, response rate, and the incidence of adverse events. Differences in these endpoints were assessed in each of the Kadcyła-containing treatment arms compared to the Herceptin plus chemotherapy arm, and also between the two Kadcyła-containing arms.

### **About Kadcyła**

Kadcyła is one of three targeted medicines that Roche has developed for the treatment of HER2-positive breast cancer. It is a type of medicine called an antibody-drug conjugate (ADC), combining two anti-cancer properties: the HER2-targeting properties of trastuzumab (the active ingredient in Herceptin) and the cytotoxic chemotherapy agent DM1. In Kadcyła, trastuzumab and DM1 are joined together using a 'stable linker' to deliver DM1 directly to HER2-positive cancer cells. Roche licenses technology for Kadcyła under an agreement with ImmunoGen, Inc.

### **About Perjeta**

Perjeta is a medicine that targets the HER2 receptor, a protein found on the outside of many normal cells and in high quantities on the outside of cancer cells in HER2-positive cancers. Perjeta is designed specifically to prevent the HER2 receptor from pairing (or “dimerizing”) with other HER receptors (EGFR/HER1, HER3 and HER4) on the surface of cells, a process that is believed to play a role in tumor growth and survival. Binding of Perjeta to HER2 may also signal the body’s immune system to destroy the cancer cells. The mechanisms of action of Perjeta and Herceptin are believed to complement each other, as both bind to the HER2 receptor, but to different places. The combination of Perjeta and Herceptin is thought to provide a more comprehensive blockade of HER signaling pathways, thus preventing tumor cell growth and survival.

### **About Roche’s medicines for HER2-positive breast cancer**

Roche has been leading research into the HER2 pathway for over 30 years and is committed to improving the health, quality of life and survival for people with both early and advanced HER2-positive disease.

Roche has developed three innovative medicines that have helped transform the treatment of HER2-positive breast cancer: Herceptin, Perjeta and Kadcyla. HER2-positive breast cancer is a particularly aggressive form of the disease that affects approximately 20 percent of patients. Over the past 15 years, the outlook for people with HER2-positive disease has improved to the extent that those with this form of the disease treated with these innovative medicines now typically experience better outcomes than people with less aggressive HER2-negative disease.

Eligibility for treatment with Roche’s HER2-targeted medicines is determined via a diagnostic test, saving time from the outset by identifying those patients who will likely benefit from these medicines.

### **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, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in *in vitro* diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche’s personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. Twenty-four medicines developed by Roche are included in the World Health Organisation Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and chemotherapy.

In 2013 the Roche Group employed over 85,000 people worldwide, invested 8.7 billion Swiss francs in R&D and posted sales of 46.8 billion Swiss francs. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit [www.roche.com](http://www.roche.com).

All trademarks used or mentioned in this release are protected by law.

#### **Additional information**

- Roche in Oncology: [www.roche.com/media/media\\_backgrounder/media\\_oncology.htm](http://www.roche.com/media/media_backgrounder/media_oncology.htm).
- Follow us via @roche on Twitter and on LinkedIn at <https://www.linkedin.com/company/1602>.

#### **Roche Group media relations**

Phone: +41 -61 688 8888 / e-mail: [basel.mediaoffice@roche.com](mailto:basel.mediaoffice@roche.com)

- Nicolas Dunant (Head)
- Ulrike Engels-Lange
- Štěpán Kráčala
- Nicole Rüppel
- Claudia Schmitt
- Nina Schwab-Hautzinger

#### **References**

1. Roche data on file.
2. U.S. National Institutes of Health. Available at: <https://clinicaltrials.gov/ct2/show/NCT01120184>.