Media Release

Basel, 20 September 2013

CHMP grants positive opinion for Roche's Kadcyla, the first antibody-drug conjugate for advanced HER2-positive breast cancer

- **Kadcyla helped extend the life expectancy of people with previously treated advanced disease to more than two and a half years overall in a Phase III clinical study**
- **Kadcyla's mode of action aims to preserve quality of life as it delivers chemotherapy directly to cancer cells, limiting damage to healthy tissues**
- **European Commission decision is expected by the end of the year**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Union's (EU) Committee for Medicinal Products for Human Use (CHMP) has recommended approval of Kadcyla (trastuzumab emtansine or T-DM1) as a single agent, for the treatment of adult patients with HER2-positive, unresectable locally advanced or metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination.

"Kadcyla's highly effective, targeted mode of action offers patients a chance to extend their lives with fewer of the side effects commonly experienced with chemotherapy," said Hal Barron, M.D., Roche's Chief Medical Officer and Head, Global Product Development. "We hope that this new medicine is soon available to patients with metastatic breast cancer in Europe."

There is currently no cure for metastatic breast cancer (mBC) and as such the aim of treatment is to help patients to live as long and as well as possible. HER2-positive mBC is currently treated with regimens comprising both targeted agents and chemotherapy. Some of the side effects commonly associated with standard chemotherapy can significantly impact patients' quality of life and may lead some to need to switch treatment or even stop treatment altogether.[1]

The CHMP opinion is based on clinical data from the international, Phase III EMILIA study which found that Kadcyla helped people with HER2-positive locally advanced or metastatic breast cancer who had

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previously been treated with Herceptin and a taxane chemotherapy to live for nearly 10 months (9.6 months) without their disease getting worse and extended their life expectancy to more than two and a half years overall (30.9 months).[2] Kadcyla has also demonstrated a tolerable safety profile and is associated with fewer of the severe side effects usually experienced with current chemotherapy known to impact patients' daily lives.[2,3]

Kadcyla is an HER2-targeted therapy that connects two anti-cancer properties: the HER2 inhibition of trastuzumab (the active ingredient found in Herceptin) and the cytotoxic chemotherapy, DM1. The trastuzumab and the DM1 are joined together using a 'stable' linker to deliver DM1 directly to HER2-positive breast cancer cells.

Kadcyla efficacy in HER2-positive mBC

The EU filing of Kadcyla is based on results from EMILIA (TDM4370g/BO21977), an international, Phase III, randomised, open-label study comparing Kadcyla alone to lapatinib in combination with Xeloda in 991 patients with HER2-positive locally advanced breast cancer or mBC who had previously been treated with Herceptin and a taxane chemotherapy. Results include:[2]

Study arms	**Kadcyla**	**Lapatinib and Xeloda**
OS **(co-primary endpoint)**	5.8 months difference HR=0.682 (95% CI: 0.548-0.849) 32% reduction in the risk of dying Observed 23% improvement in median OS p=0.0006	
Median OS	30.9 months	25.1 months
PFS **(co-primary endpoint, independent review)**	3.2 months difference HR=0.650 (95% CI: 0.549-0.771) 35% reduction in the risk of disease worsening or death Observed 50% improvement in median PFS p<0.0001	
Median PFS	9.6 months	6.4 months
Response rate **Median duration of response**	43.6% 12.6 months	30.8% 6.5 months
Safety profile	Kadcyla showed a tolerable safety profile	
Rate of Grade 3 or	43.1%	59.2%

higher AEs **Most common Grade 3 or higher AEs**	For people receiving Kadcyla, the most common (occurring in more than 2% of patients) Grade 3 or higher AEs were: Thrombocytopenia (12.9%), elevated AST (4.3%), elevated ALT (2.9%), anaemia (2.7%), fatigue (2.4%), hypokalaemia (2.2%) and neutropenia (2%).	For people receiving Lapatinib and Xeloda, the most common (occurring in more than 2% of patients) Grade 3 or higher AEs were: Diarrhoea (20.7%), hand and foot syndrome (16.4%), vomiting (4.5%), neutropenia (4.1%), fatigue (3.5%), nausea (2.5%) and mucosal inflammation (2.3%).

About Roche's medicines for HER2 positive disease

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 patients with both early and metastatic stage HER2-positive disease.

Roche has developed a number of innovative medicines which have helped transform the treatment of HER2-positive breast cancer. HER2-positive breast cancer is a particularly aggressive form of the disease which affects approximately 20 percent of patients. Over the past 15 years the outlook for patients with HER2 disease has improved to the extent that patients with the disease experience better outcomes than those of patients with HER2-negative disease.

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

Roche licenses technology for Kadcyla under an agreement with ImmunoGen, Inc.

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, infectious diseases, inflammation, metabolism 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 diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2012 Roche had over 82,000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 45.5 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.

Additional information

Roche in Oncology: www.roche.com/de/media/media_backgrounder/media_oncology.htm

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