Roche’s Herceptin given by subcutaneous injection offers greater convenience to patients and reduces overall healthcare costs compared to standard IV infusion

Subcutaneous administration of Herceptin is less invasive and takes approximately 5 minutes instead of 30-90 minutes with currently approved IV administration

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced results from the Phase III HannaH study in women with HER2-positive early breast cancer (eBC) showing for the first time that a new way of giving Herceptin (trastuzumab) by subcutaneous (SC) injection leads to comparable efficacy (based on pathological complete response (pCR); complete eradication of the tumour cells in the breast) to the current way of giving the medicine by intravenous (IV) route. Herceptin SC may provide greater convenience to patients versus the traditional IV method due to its less invasive administration route and quicker administration time (5 minutes versus 30 – 90 minutes). The HannaH study also demonstrated Herceptin SC had comparable mean concentrations of Herceptin in the blood (pharmacokinetics; PK) versus the IV formulation. The overall safety profile in both arms of the HannaH study was consistent with that expected from treatment with Herceptin and standard chemotherapy in this setting. The results were presented today at the 8th European Breast Cancer Conference (EBCC-8) in Vienna (Abstract # 1BA) as part of the EBCC-8 keynote symposium session.

“The subcutaneous formulation of Herceptin provides an alternative to intravenous Herceptin and is an important treatment option for patients with HER2 positive breast cancer,” said Hal Barron, M.D., Chief Medical Officer and Head, Global Product Development. “Because it is less invasive and takes 5 rather than 30-90 minutes to administer, subcutaneous Herceptin is more convenient for patients and may reduce healthcare costs relative to the standard intravenous formulation.”

The SC administration is a less invasive administration process than the IV infusion and may allow patients to spend less time in hospital receiving their Herceptin treatment compared with the IV method. This is important in the eBC setting where Herceptin is usually given for 1 year. Herceptin SC is given as an injection under the skin at a fixed dose of 600 mg. In contrast to IV Herceptin, a loading dose and weight-adjusted dosing are not required for the SC formulation and the same dose is used irrespective of patient’s
body weight.

Based on the HannaH data, Roche has submitted a Line Extension Application for Herceptin SC to the European Medicines Agency (EMA), for the treatment of HER2-positive breast cancer.

The co-primary endpoints of PK and efficacy met their pre-specified criteria. The drug concentration in the blood measured just before surgery was at least as high for the SC as for the IV formulation (69.0 and 51.8 μg/mL, respectively). This is important in order to demonstrate comparable efficacy. In addition, efficacy, determined by pCR, in patients treated in the SC arm was in the same range as in patients who received the IV formulation (45.4 percent and 40.7 percent, respectively).

All-grade adverse events (AEs) and severe AEs were comparable between arms. The most frequent AEs in either arm (above 25% in either arm) were alopecia, nausea, neutropenia, diarrhoea, asthenia and fatigue. More adverse events were reported as serious in the SC arm but no specific clinical explanation (e.g. from underlying patient or drug characteristics) for this finding was detected.

**About subcutaneous delivery**

Herceptin SC is a new more convenient formulation of Herceptin that uses Enhanze™ Technology, developed by Halozyme Therapeutics, Inc. which contains the novel excipient (carrier for active ingredients of a medication), rHuPH20. rHuPH20 (recombinant human hyaluronidase) reversibly breaks down a gel-like substance (hyaluronan) that forms a barrier in the tissues between cells under the skin. This facilitates the distribution of injected volumes over a greater area and enables painless subcutaneous administration of the large volume of Herceptin SC (a fixed dose of 600 mg (5ml)).

**About the HannaH study**

HannaH is a Phase III, randomised, open-label, international, multicentre study. A total of 596 patients with operable or locally advanced eBC were enrolled. The study investigated the efficacy, pharmacokinetics and safety of Herceptin SC (in a ready-to-use vial) and Herceptin IV in the neoadjuvant–adjuvant treatment setting (given before and after surgical intervention) of women with HER2-positive eBC. Treatment duration was 1 year in total for both arms. The co-primary endpoints were:

- Pharmacokinetics (PK).
- Pathologic complete response (pCR).
Main secondary endpoints were:

- Safety and tolerability
- pCR in the breast and axilla (tpCR).
- Event free survival (EFS) and overall survival (OS).

Participants in the Herceptin SC arm received:

- 600 mg (fixed dose) of Herceptin SC plus chemotherapy for 8 cycles before surgery.
- Herceptin SC alone for 10 cycles after surgery.

Participants in the Herceptin IV arm received:

- An initial 8 mg/kg body weight loading dose of Herceptin IV followed by 6 mg/kg maintenance dose both in combination with chemotherapy for a total of 8 cycles before surgery, as per the standard IV regimen.
- Herceptin IV alone for 10 cycles after surgery.

Adverse Events (AEs) in the study were consistent with the known Herceptin safety profile. No new safety signals were identified. Overall, the incidence of most common AEs (above 10% in either arm) was comparable. Severe AEs (grade >3) occurred at a similar incidence between arms (52 percent for Herceptin IV and 51.9 percent for Herceptin SC). Cardiac adverse events were similar in both treatment arms: 12.1 percent vs. 11.4 percent in the IV and SC arms respectively. 11 percent of patients who received the SC injection experienced an injection site reaction (most commonly pain at the site of injection) which was mild in intensity in 95 percent of patients.

**Clinical trials - SC**

Two additional Herceptin SC studies are currently ongoing. PrefHer is a randomised, multi-centre, multinational cross-over study to evaluate patient preference and healthcare professional satisfaction with SC administration of Herceptin as an adjuvant therapy in patients with HER2-positive eBC. PrefHer is a two cohort study (involving 400 patients in total) comparing Herceptin SC administration, via vial or an innovative ready-to-use device, with Herceptin IV administration. The ready-to-use injection device is an important advance as it could eventually allow patients to self-administer Herceptin. Data is expected in 2013.

SafeHer is a two-cohort multinational and open label study to assess the safety of assisted- and self-administered SC Herceptin as an adjuvant therapy in patients with operable HER2-positive eBC. The study
allows the use of both vial administration and administration via the ready-to-use device with the option of self-administration.

Roche are also investigating the use of MabThera (rituximab) for subcutaneous injection in non-Hodgkin’s lymphoma and chronic lymphocytic leukaemia. MabThera for subcutaneous injection is not currently licensed or approved in any market. Roche anticipates an initial EU filing in late 2012.

About breast cancer
Breast cancer is the most common cancer among women worldwide. Each year about 1.4 million new cases of breast cancer are diagnosed worldwide, and over 450,000 women will die of the disease annually. In HER2-positive breast cancer, increased quantities of the human epidermal growth factor receptor 2 (HER2) are present on the surface of the tumour cells. This is known as “HER2 positivity” and affects approximately 15-20 percent of women with breast cancer. HER2-positive cancer is a particularly aggressive form of breast cancer.

About Herceptin
Herceptin (trastuzumab) is a humanised monoclonal antibody, designed to target and block the function of HER2, a protein produced by a specific gene with cancer-causing potential when it is overexpressed. The mode of action of Herceptin is unique in that it activates the body’s immune system and suppresses HER2 signalling 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 overall survival, response rates and disease-free 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 almost 1 million people 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 2010, Roche had over 80'000 employees worldwide and invested over 9 billion Swiss francs in R&D. The Group posted sales of 47.5 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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References