Basel, 20 June 2011

Pivotal study showed vismodegib helped shrink tumours or heal lesions in people with rare form of advanced skin cancer

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that a pivotal Phase II study with vismodegib showed positive results in people with advanced basal cell carcinoma (BCC) for whom surgery is considered inappropriate. Basal Cell Carcinoma is a form of skin cancer that can cause disfiguring and debilitating effects and can ultimately be life-threatening. Vismodegib is an investigational, oral medicine designed to selectively inhibit signalling in the Hedgehog pathway, which is implicated in more than 90 percent of BCC cases.¹

The trial showed vismodegib substantially shrank tumours or healed visible lesions (overall response rate) in 43 percent of patients with locally advanced BCC (laBCC) and 30 percent of patients with metastatic BCC (mBCC), as assessed by independent review, the primary endpoint. The most common drug related adverse events were muscle spasms, hair loss, altered taste sensation, weight loss, fatigue, nausea, decreased appetite and diarrhoea.

“Vismodegib is an example of our commitment to understanding and developing medicines that target the biologic cause of a particular disease,” said Hal Barron, M.D., Chief Medical Officer and Head, Global Product Development. “Our goal is to provide a medicine to people with this rare and disfiguring form of advanced skin cancer as soon as possible, and we are discussing these results with global regulatory authorities.”

Full results of the study will be presented tomorrow at the Seventh European Association of Dermato-Oncology (EADO) Congress taking place in Nantes, France (Abstract C014,14:50. CET).
In order to provide people with advanced BCC (who are appropriate candidates) access to vismodegib while Roche discusses next steps with the European Medicines Agency, the company is conducting a phase II safety study in the EU and other countries. For more information, please access www.rochetrials.com.

**About the Phase II Trial (ERIVANCE BCC/SHH4476g)**

ERIVANCE BCC is an international, single-arm, multi-centre, two-cohort, open-label Phase II study that enrolled 104 patients with advanced BCC, including laBCC (71) and mBCC (33). laBCC patients had lesions that were inappropriate for surgery (inoperable, or for whom surgery would result in substantial deformity) and for which radiotherapy was unsuccessful or contraindicated. mBCC was defined as BCC that had spread to other parts of the body, including the lymph nodes, lung, bones and/or internal organs. The 31 study sites were located in the US, Australia and Europe. Study participants received 150mg vismodegib orally, once daily until disease progression or intolerable toxicity.

The primary endpoint of the trial showed an overall response rate of 43 percent in the laBCC cohort, and 30 percent in mBCC, as assessed by independent review. Study investigators assessed the overall response rate for laBCC and mBCC at 60 percent and 46 percent, respectively (secondary endpoint). The median duration of progression-free survival (PFS) by independent review for both metastatic and locally advanced BCC patients was 9.5 months.

In addition, the clinical benefit rate (defined as patients who experienced response as well as those who experienced prolonged stable disease for more than 24 weeks) showed vismodegib shrunk tumours or healed visible lesions, or prevented them from growing any further in 75 percent of patients, as assessed by independent review.

The most common adverse events included muscle spasms, hair loss, altered taste sensation, weight loss, fatigue, nausea, decreased appetite and diarrhoea. Serious adverse events (SAEs) were observed in 26 patients (25 percent), however of these only four (4 percent) patients had SAEs that were considered to be related to treatment with vismodegib. Fatal events were reported in seven patients (7 percent); none were considered by investigators to be related to treatment with vismodegib. In all cases, patients had other pre-existing diseases
or symptoms that were related to their presumed cause of death.

**About Basal Cell Carcinoma**

BCC is the most common type of skin cancer in Europe, Australia and the USA. The annual global incidence is more than 2 million cases. Currently, there are limited treatment options for advanced BCC with no current standard of care. In the majority of cases, the disease is generally considered curable if the cancer is restricted to a small area of the skin. However, in a very small group of people, if the disease is left untreated or recurs after surgery, the cancer may invade further into surrounding tissues such as sensory organs (ears, nose and eyes), bones or other tissues (laBCC). In a small proportion of patients (estimated at less than 1 percent of those affected), BCC can advance or spread to other parts of the body (mBCC). Advanced BCC can be difficult to treat with current treatments and can be life-threatening.

**Vismodegib (RG3616/GDC-0449)**

Vismodegib is an investigational medicine designed to target the underlying molecular driver of BCC. Abnormal signalling in a cell growth pathway, known as the Hedgehog pathway, is implicated in more than 90 percent of BCC cases and vismodegib is designed to selectively inhibit abnormal signaling in the Hedgehog pathway. Roche is also evaluating vismodegib in a Phase II trial in people with operable forms of BCC.

Roche is developing vismodegib under a collaboration agreement with Curis, Inc. Vismodegib was discovered by Genentech and jointly validated by Genentech and Curis through a series of preclinical studies. Through this collaboration, Genentech (U.S.), Roche (ex-U.S. excluding Japan) and Chugai Pharmaceuticals (Japan) are responsible for the clinical development and commercialisation of vismodegib. Curis is eligible to receive cash payments upon the successful achievement of specified clinical development and regulatory approval milestones, as well as royalties upon commercialisation of vismodegib.

**Roche and Personalised Healthcare (PHC)**

Roche’s Personalised Healthcare strategy aims to provide medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. It is an approach that capitalises on our
extensive knowledge of the molecular basis of diseases and how medicines work, as well as on our increasingly sophisticated understanding of patients’ biological differences. The aim of PHC is to ensure that the right patients get the right medicine – either by employing a diagnostic to determine if the patient has the specific mutation in question, or by designing a drug that works on a specific mutation that exists in most tumours.

**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](http://www.roche.com).

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