Basel, 3 June 2012

Roche data showed that people with metastatic colorectal cancer lived longer when they continued on Avastin plus chemotherapy
First phase III study to appraise continued Avastin through different lines of therapy

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced results from ML18147, a phase III study in metastatic colorectal cancer (mCRC) that evaluated Avastin (bevacizumab) continued with second-line chemotherapy in people who received initial Avastin plus first-line chemotherapy.

The study met its primary endpoint of a significant increase in overall survival (OS). In the study, the relative risk of death was reduced by 19 percent for people who continued with Avastin plus second-line chemotherapy compared with those who received chemotherapy alone (HR = 0.81, p = 0.0062). People who continued with Avastin plus second-line chemotherapy also experienced a significant improvement in progression free survival (PFS, the time a person lives without the disease getting worse); the risk of their cancer progressing was reduced by 32 percent (HR = 0.68, p<0.0001). Adverse events in ML18147 were consistent with those seen in previous pivotal trials of Avastin across tumour types.

“Our study design was based on previous research showing that sustained VEGF inhibition achieved and maintained anti-tumour activity,” said Hal Barron M.D., chief medical officer and head, Global Product Development. “While conventional practice is to change treatment completely at disease progression, the continued use of Avastin with a new chemotherapy regimen in this study resulted in patients living longer, compared to a new chemotherapy regimen alone.”

These results were featured in a press briefing on Saturday, June 2nd at the 48th Annual Meeting of the American Society of Clinical Oncology. Full results will be presented in the ASCO Gastrointestinal (Colorectal) Cancer Oral Abstracts session by Professor Dirk Arnold, Hubertus Wald Tumor Center at the University Cancer Center Hamburg of the University Clinic Hamburg-Eppendorf, Germany (Abstract CRA3503, Sunday, June 3, 10:45 a.m. CDT).
**ML18147 Study Results**

- People with mCRC who received Avastin in combination with standard chemotherapy in both the first- and second-line settings had a median OS of 11.2 months compared to 9.8 months for people who received chemotherapy alone.
- Median PFS was 5.7 months compared to 4.1 months.
- OS and PFS were calculated from the time patients were randomised to the second-line treatment.

**About the ML18147 study**

ML18147 was a randomised, open-label phase III multicentre, multinational trial evaluating the efficacy and safety profile of Avastin plus standard second-line chemotherapy in 820 patients with mCRC whose disease had progressed following Avastin plus standard first-line chemotherapy (irinotecan or oxaliplatin-based).

Patients were randomised at progression to one of two treatment arms:

- Arm A: Chemotherapy* plus Avastin (equivalent of 2.5 mg/kg i.v. per week)
- Arm B: Chemotherapy* alone

*Depending on the first-line chemotherapy backbone (fluoropyrimidine / irinotecan-based or fluoropyrimidine / oxaliplatin-based) the chemotherapy backbone was switched in the second-line setting.

The primary endpoint of the study was overall survival measured from the time patients were randomised to the second-line treatment. The secondary efficacy endpoints of the study included PFS, overall response rate and safety profile.

**About metastatic Colorectal Cancer (mCRC)**

Colorectal cancer is one of the most common cancers in the world, with over 1.2 million new cases diagnosed each year; it is the second most common cancer in women and the third most common cancer in men.¹ Despite improvements in screening for early diagnosis, colorectal cancer remains one of the biggest cancer killers in the world and is responsible for over 600,000 deaths each year.¹ ²

In general the current treatment options for colorectal cancer are surgery, chemotherapy, and biological therapies. Early-stage (localised) cancer has the potential to be cured if the tumour can be successfully surgically removed. Patients with advanced (metastatic) disease are usually treated with chemotherapy after surgery, known as ‘first-line’ treatment. Many people initially respond to chemotherapy, but unfortunately, in the majority of cases the disease eventually progresses after first-line treatment and patients may require a
further round of treatment ('second-line'). There is therefore a real need for effective, tolerable treatments for long-term disease control in metastatic colorectal cancer.

**About Avastin: Over 7 Years of Transforming Cancer Care**
With the initial approval in the USA for advanced colorectal cancer in 2004, Avastin became the first anti-angiogenic therapy made widely available for the treatment of patients with an advanced cancer.

Today, Avastin is continuing to transform cancer care through its proven survival benefit (overall survival and/or progression free survival) across several types of cancer. Avastin is approved in Europe for the treatment of advanced stages of breast cancer, colorectal cancer, non-small cell lung cancer, kidney cancer and ovarian cancer, and is available in the US for the treatment of colorectal cancer, non-small cell lung cancer and kidney cancer. In addition, Avastin is approved in the US and over 30 other countries for the treatment of patients with glioblastoma (a type of brain cancer). Avastin is approved in Japan for the treatment of the advanced stages of colorectal, non-small cell lung cancer and breast cancer. Avastin is the only anti-angiogenic therapy available for the treatment of these numerous advanced cancer types, which collectively cause over 2.5 million deaths each year.

Avastin has made anti-angiogenic therapy a fundamental pillar of cancer treatment today – over one million patients have been treated with Avastin so far. A comprehensive clinical programme with more than 500 ongoing clinical trials is investigating the use of Avastin in over 50 tumour types.

**About Avastin: Mode of Action**
An independent blood supply is critical for a tumour to grow beyond a certain size (2mm) and spread (metastasise) to other parts of the body. Tumours develop their own blood supply in a process called angiogenesis by releasing vascular endothelial growth factor (VEGF) – a key driver for tumour growth. Avastin is an antibody that precisely targets and inhibits VEGF for continuous tumour control. Avastin's precise VEGF inhibition allows it to be combined effectively with a broad range of chemotherapies and other anti-cancer treatments with limited additional impact on the side effects of these therapies.

**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 2011, Roche had over 80,000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 42.5 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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