Roche announces final phase III study results of Avastin plus radiotherapy and chemotherapy in people with an aggressive form of brain cancer

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced final results from the phase III AVAglio study in people with newly diagnosed glioblastoma, the most common and aggressive form of primary brain cancer. Final results confirmed people who received Avastin (bevacizumab) plus radiotherapy and temozolomide chemotherapy benefited from a significant improvement in progression-free survival (PFS) compared to those who received placebo plus radiotherapy and temozolomide chemotherapy. Overall survival (OS) was not significantly improved in the study.

As previously announced, Avastin plus radiotherapy and temozolomide chemotherapy significantly reduced the risk of the glioblastoma worsening or death by 36 percent compared to radiotherapy and temozolomide chemotherapy plus placebo (PFS as assessed by trial investigators, a co-primary endpoint: HR=0.64; p<0.0001, median PFS 10.6 months versus 6.2 months, respectively). People who received Avastin plus radiotherapy and temozolomide chemotherapy did not have a statistically significant improvement in OS (the other co-primary endpoint), compared to those who received radiotherapy and temozolomide chemotherapy plus placebo (HR=0.88; [95% CI 0.76, 1.02], p=0.0987). Median survival was similar in both arms (16.8 months versus 16.7 months, respectively). No new safety findings were observed in the AVAglio study and adverse events were consistent with those seen in previous trials of Avastin across tumour types for approved indications.

“We continue to be encouraged that people with newly diagnosed glioblastoma who received Avastin plus radiotherapy and temozolomide chemotherapy in the study experienced a significantly longer period of time without their cancer worsening,” said Hal Barron MD, Chief Medical Officer and Head of Roche Global Product Development. “While the study did not show a significant increase in overall survival, delaying disease progression is considered to be an important goal for people with this aggressive brain cancer who have very limited treatment options. We will discuss these data with regulatory authorities.”
The symptoms of glioblastoma are often distressing to patients and their caregivers as they significantly and negatively impact on quality of life as well as ability to carry out activities of daily living. The study also showed that during the progression free time most patients were able to care for themselves without requiring assistance and maintain clinically relevant health-related quality of life measures.

The results of the phase III AVAglio trial were presented today at the 49th Annual Meeting of the American Society of Clinical Oncology (ASCO) in the Central Nervous System Tumors Session by Professor Wolfgang Wick, M.D., Professor of Neurology, Chairman of the Division of Neuro-oncology at the Neurology Centre at Heidelberg University Hospital, Germany (Abstract 2002, Saturday, June 1, 3:30 P.M. Central Time).

Currently, Avastin is approved in over 60 countries worldwide for the treatment of patients with progressive glioblastoma following prior therapy. In addition, applications for first line-treatment have been filed with regulatory bodies in the EU, Switzerland as well as Japan.

**Additional AVAglio study results**

Secondary endpoints:
- An independent review committee assessment of PFS showed a 39 percent reduction in the risk of disease worsening or death, which can also be referred to as a 64 percent improvement in PFS (HR=0.61; p<0.0001; median PFS 8.4 months versus 4.3 months). This was consistent with the magnitude of benefit assessed by the trial investigators.
- Seventy-two percent of people treated in the Avastin arm were alive at one year compared to 66 percent of people in the placebo arm (p=0.049). Thirty-four percent were alive at two years compared to 30 percent, respectively (p=0.235).
- Health-related quality of life measures including global health status and physical, social and motor functioning, as well as communication deficit, remained stable or improved in most patients in both arms of the trial during the time from diagnosis to disease progression.
- No new safety findings were observed in the AVAglio study and adverse events were consistent with those seen in previous trials of Avastin across tumour types for approved indications.

**About the AVAglio study**

AVAglio is a Phase III, randomised, double-blind, placebo controlled trial that assessed the efficacy and safety profile of Avastin in combination with radiotherapy and temozolomide chemotherapy following surgery or biopsy in patients with newly diagnosed glioblastoma. Patients were randomised to one of two arms:
• Avastin plus radiotherapy and temozolomide chemotherapy for six weeks followed by a four-week break. Patients then received Avastin and temozolomide chemotherapy for up to six cycles, followed by Avastin alone until disease progression.

• Radiotherapy, temozolomide chemotherapy and placebo for six weeks followed by a four-week break. Patients then received temozolomide chemotherapy and placebo for up to six cycles, followed by placebo until disease progression.

The co-primary endpoints of the study were OS and PFS as assessed by trial investigators. Secondary endpoints included PFS as assessed by an independent review committee, one- and two-year survival rates, health-related quality of life measures, and safety profile.

About glioblastoma

Glioma (cancer of the glial cells) is the most common type of malignant primary brain tumour (a tumour that originates in the brain), accounting for approximately one third of all cases diagnosed1. Glioblastoma (or glioblastoma multiforme) is the most common and the most aggressive type of glioma1. Globally, the incidence of glioblastoma is approximately 1 to 2 in 100,000 people annually1,2. Glioblastoma has among the highest levels of vascular endothelial growth factor (VEGF) of any solid tumour.

About Avastin – over 9 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 over 60 other countries worldwide for the treatment of patients with progressive glioblastoma following prior therapy. 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. Precise VEGF inhibition by Avastin 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, 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.

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
- Roche at ASCO: http://www.roche.com/media/roche_stories/asco-2013-overview.htm
References