Roche’s Avastin approved in Japan for treatment of the most aggressive form of brain cancer
First approval of Avastin for the treatment of newly diagnosed glioblastoma

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the Japanese Ministry of Health, Labour and Welfare (MHLW) has approved Avastin (bevacizumab) for the treatment of malignant glioma, including newly diagnosed glioblastoma (GBM) in combination with radiotherapy and temozolomide chemotherapy, and as monotherapy for treatment of recurrent GBM and certain other types of high grade glioma following prior therapy. Current treatment options for malignant glioma are limited, and Avastin represents the first new medicine approved worldwide for newly diagnosed glioblastoma, the most common and aggressive form of primary brain cancer, in the last eight years.

“This approval of Avastin is important news for people in Japan who have been diagnosed with glioma and glioblastoma because aggressive brain cancer can significantly reduce a person’s quality of life and the ability to perform everyday activities,” said Hal Barron MD, Roche’s Chief Medical Officer and Head of Global Product Development. “People with newly diagnosed glioblastoma who received Avastin plus radiotherapy and temozolomide chemotherapy in the pivotal study experienced a significantly longer period of time without their cancer worsening.”

The approval was based on data from three clinical studies in GBM:

- The phase II BRAIN study
- A Japanese phase II study (JO22506)
- The pivotal phase III AVAglio study, which demonstrated that when Avastin was added to standard treatment, patients lived significantly longer without their disease getting worse.

Final results from the AVAglio study in newly diagnosed GBM patients were recently presented at the 49th annual meeting of the American Society of Clinical Oncology in Chicago.
Applications for first-line treatment have been filed with the health authorities in the EU and Switzerland. Avastin is marketed in Japan by Chugai Pharmaceutical, a member of the Roche Group. Avastin for malignant glioma was designated as an orphan drug in Japan in May 2013, as the estimated number of newly diagnosed malignant glioma and GBM patients per year is about 1,700.

**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.

**AVAglio study results**

- 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 vs. 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 vs. 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 tumor types for approved indications.
- 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.
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 diagnosed. Glioblastoma (or glioblastoma multiforme) is the most common and the most aggressive type of glioma. Globally, the incidence of glioblastoma is approximately 1 to 2 in 100,000 people annually. Current treatment options for GBM are very limited. Generally, patients’ tumours get worse within the first 6 months of initial therapy and the median overall survival of patients following diagnosis is 15 months. Glioblastoma has among the highest levels of vascular endothelial growth factor (VEGF) expression of any solid tumour, which led to the rationale to investigate the effect of anti-angiogenic therapies on this disease.

About Avastin – over nine 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 60 other countries worldwide for the treatment of patients with progressive glioblastoma following prior therapy. The approval in the USA was granted under the Food and Drug Administration’s (FDA) accelerated approval program. 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.

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**Additional information**

- Roche in Oncology: [www.roche.com/media/media_backgrounder/media_oncology.htm](http://www.roche.com/media/media_backgrounder/media_oncology.htm)

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**References**

