

Basel, 20 November 2009

## European medical advisory committee does not recommend approval of Avastin for deadly form of brain cancer

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the Committee for Medicinal Products for Human Use (CHMP), which is responsible for conducting the initial assessment of medicinal products that have been filed for marketing authorisation in Europe, has issued a negative opinion relating to the approval of Avastin (bevacizumab) alone or in combination with irinotecan chemotherapy for the treatment of relapsed or progressive glioblastoma (GBM), the most aggressive type of primary malignant brain cancer. The filing was based on results from the phase II BRAIN study (AVF3708g)<sup>1</sup>.

The major objection from the CHMP was the lack of a comparator arm without Avastin in the BRAIN study, an investigational phase II trial. The CHMP tends to base its approval decisions on Phase III studies only. Roche decided to submit this data set to regulatory authorities globally based on Avastin's remarkable clinical activity seen in BRAIN. Roche remains convinced that the results of the BRAIN study, which were published in the *Journal of Clinical Oncology* in October 2009<sup>1</sup> are robust and remain valid. Adverse events in the BRAIN study were consistent with those previously seen with Avastin and no new safety signals were reported.<sup>1</sup>

"We are very disappointed with the CHMP opinion which will result in a delay to patients receiving an important new treatment option. We strongly believe that Avastin is a new treatment option for physicians within the EU which would bring hope to GBM patients and their families as it is today in the US and other countries," said William M. Burns, CEO of Roche's Pharmaceuticals Division. "Relapsed glioblastoma is a rare condition and represents a very high unmet medical need. These patients deserve effective additional therapies to manage this devastating disease. We remain committed to bringing Avastin to patients with newly diagnosed GBM in Europe".

In May 2009 Avastin was granted accelerated approval for the treatment of GBM patients with progressive disease following prior therapy from the US Food and Drug Administration (FDA) based on data from the

BRAIN study (AVF3708g) and an NCI study (NCI 06-C-0064E). Switzerland and ten other countries have already recognised the significant clinical benefits Avastin offers to GBM patients by giving approval.

Roche continues to further explore the role of Avastin in GBM through various investigator-led studies. In addition, a large phase III study (AVAGLIO) in over 900 patients with newly diagnosed GBM is currently underway with the aim of a global filing<sup>5</sup>.

Avastin has proven survival benefits across several types of cancer. It is approved in Europe for the treatment of the advanced stages of four common types of cancer: colorectal cancer, breast cancer, non-small cell lung cancer (NSCLC) and kidney cancer. These types of cancer collectively cause over 2.5 million deaths each year<sup>6,7,8</sup>. Over half a million patients have been treated with Avastin so far.

### **About Glioblastoma**

Glioma is the most common type of primary brain tumour, accounting for approximately one third of all cases diagnosed<sup>9</sup>. Glioma also represents around 80% of all primary malignant brain tumour cases<sup>9</sup>.

Glioblastoma (or glioblastoma multiforme; GBM) is the most common and the most aggressive type of glioma<sup>9</sup>. The prognosis for patients with GBM is poor. The treatment options for GBM depend on many factors including the location and size of the tumour, and the overall health and age of the patient<sup>10</sup>.

Glioblastoma affects approximately 17,000 people per year in the EU<sup>2</sup>. Following initial treatment, glioblastoma tumours nearly always return and currently, there are limited treatment options for patients when these relapses occur and their prognosis is particularly poor<sup>3</sup>. According to historical estimates, less than 10 percent of patients with recurrent GBM respond to treatment and approximately 15 percent will live six months without their disease getting worse<sup>1,5</sup>. GBM is a compelling therapeutic target for Avastin as these tumours have very high levels of vascular endothelial growth factor (VEGF)<sup>11</sup>.

### **About the BRAIN study (AVF3708g)**

The BRAIN study was a US based open-label, multicentre, non-comparative phase II study including 167 patients with histologically confirmed GBM that had progressed following initial treatment with temozolomide and radiation. The primary endpoints of the BRAIN trial were progression free survival-6 (PFS-6), (defined as the percentage of patients who remained alive and progression free at 24 weeks) and objective response rate (ORR), (defined as a complete or partial response on two consecutive MRIs obtained 4 weeks apart). Secondary endpoints explored included OS, PFS, duration of response to treatment and

safety. The BRAIN study evaluated Avastin at a dose of 10mg/kg every two weeks, as a single agent (BEV), or in combination with irinotecan chemotherapy (BEV-IRI).

The BRAIN study demonstrated that:

- When Avastin was evaluated as a single agent, the study showed that at six months over 40% (42.6%) of the patients were alive without their disease getting worse, as defined by PFS-6. When Avastin was combined with irinotecan, this figure increased to 50.3%<sup>1</sup>.
- In the study, over a quarter (28%) of patients responded to Avastin as a single agent, meaning tumours decreased in size by at least 50%. When Avastin was combined with irinotecan, 38% of patients responded to Avastin<sup>1</sup>.
- Patients receiving Avastin alone had a median overall survival of 9.2 months; this was 8.7 months for those receiving Avastin in combination with irinotecan, which was a secondary endpoint in the study<sup>1</sup>.
- Adverse events in the BRAIN study were consistent with those previously seen with Avastin and no new safety signals were reported<sup>1</sup>.
- Recent results showed the potential for additional positive impact on patients' daily lives. Of those patients who responded to Avastin-based therapy, a majority had a stabilisation or improvement in neurocognitive function at the time of the response and a reduction in their dose of steroids from baseline<sup>4</sup>.

### **About the AVAGLIO study**

The AVAGLIO study is an international, multicentre, randomised, double blind, phase III study including over 900 patients with newly diagnosed histologically confirmed GBM which will investigate the efficacy and safety of treatment with Avastin combined with standard of care (temozolomide chemotherapy and radiotherapy) following surgery.

The primary endpoints of the AVAGLIO trial are progression free survival, (defined as the duration for which patient remains alive without their disease worsening) and overall survival. Secondary endpoints that will be explored include one and two year survival rates, safety and health related quality of life.

### **About Avastin**

Avastin is an antibody that specifically binds and blocks the biological effects of VEGF (vascular endothelial growth factor). VEGF is a key driver of tumour angiogenesis – an essential process required for a tumour to

grow and to spread (metastasize) to other parts of the body. Avastin's precise mode of action allows it to be combined effectively with a broad range of chemotherapies and other anti-cancer treatments. Avastin helps to control tumour growth and extend survival with only a limited impact on the side effects of chemotherapy.

Avastin has proven survival benefits across several types of cancer. It is approved in Europe for the treatment of the advanced stages of four common types of cancer: colorectal cancer, breast cancer, non-small cell lung cancer (NSCLC) and kidney cancer. These types of cancer collectively cause over 2.5 million deaths each year<sup>6,7,8</sup>. In the US, Avastin was the first anti-angiogenesis therapy approved by the FDA and it is now approved for the treatment of five tumour types: colorectal cancer, non-small cell lung cancer, breast cancer, brain (glioblastoma) and kidney (renal cell carcinoma).

Over half a million patients have been treated with Avastin so far. A comprehensive clinical programme with over 450 clinical trials is investigating the use of Avastin in various tumour types (including colorectal, breast, non-small cell lung, brain, gastric, ovarian, prostate and others) and different settings (advanced or early stage disease).

### **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 2008, Roche had over 80,000 employees worldwide and invested almost 9 billion Swiss francs in R&D. The Group posted sales of 45.6 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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### **Additional information**

- About cancer: [www.roche.com/cancer.htm](http://www.roche.com/cancer.htm)
- B-Roll and visuals can be found at: [www.thenewsmarket.com](http://www.thenewsmarket.com)

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