

Basel, 6 May 2009

## **Important New Treatment Option Approved in US for Patients with the Most Aggressive Form of Brain Cancer**

### **FDA Grants Accelerated Approval of Avastin for Brain Cancer (Glioblastoma) that has progressed following prior therapy**

Roche today announced that the US Food and Drug Administration (FDA) granted accelerated approval of Avastin (bevacizumab) for people with glioblastoma with progressive disease following prior therapy. The new indication for Avastin was granted under the FDA's accelerated approval program that allows provisional approval of medicines for cancer or other life-threatening diseases. It follows the unanimous vote by the FDA Oncologic Drugs Advisory Committee (ODAC) on March 31<sup>st</sup>.

"People with this type of brain cancer have had no new treatments in more than a decade," said Timothy Cloughesy, M.D., director, Neuro-Oncology Program of the Jonsson Comprehensive Cancer Center at the University of California, Los Angeles. "After so many years with little progress in this field, Avastin was associated with a durable tumor response and doctors now have a new medicine to offer patients."

"Today's approval would not have been possible without the dedication of physicians, patient advocates, the FDA and most importantly the people who participated in the clinical trials and their families who had the courage to support them," said William M. Burns, CEO of Roche's Pharmaceuticals Division. "A global Phase III trial in patients with newly diagnosed glioblastoma will soon begin enrollment to further evaluate Avastin in this setting."

The National Brain Tumor Society, an American patient group, has welcomed the FDA's accelerated approval of Avastin. "A brain cancer diagnosis is devastating because the tumors invade brain tissue and can cause rapid deterioration," said Harriet Patterson, director of patient services for the National Brain Tumor Society. "Until now, people with relapsed glioblastoma have had almost no treatment choices and little hope."

Following initial treatment with chemotherapy and radiation, more than 90% of patients with glioblastoma

will see their cancer return and there are few effective treatments when the initial therapy stops working. Median survival following progression of this cancer is approximately six months.<sup>1</sup>

The effectiveness of Avastin for this aggressive form of brain cancer is based on an improvement in objective response rate from the BRAIN study (AVF3708g) and an NCI study (NCI 06-C-0064E). Currently, no data are available from randomized controlled trials demonstrating an improvement in disease-related symptoms or increased survival with Avastin in glioblastoma.

Roche has also filed an application with the EMEA in December 2008 for marketing authorisation for Avastin as a therapy for patients with previously treated glioblastoma. The BRAIN study forms the basis of both US and European regulatory submissions.

### **About the BRAIN Study**

The accelerated approval is based on independently reviewed data from the BRAIN study which was an open-label, multicenter, non-comparative Phase II study that included 167 patients with glioblastoma that had progressed following initial treatment with temozolomide and radiation. Patients were randomized into two arms: Avastin alone or Avastin in combination with irinotecan. A primary endpoint of the study was objective response rate. Response was assessed by magnetic resonance imaging (MRI) and measured using World Health Organization radiographic criteria along with decreased or stable corticosteroid use. MRI does not necessarily distinguish between the tumor, swelling (edema), or tissue death (necrosis) caused by prior radiation therapy.

In the 85 patients treated with Avastin alone, the study showed:

- In 26 percent (95% confidence interval: 17.0%, 36.1%) of patients tumor response was observed;
- In patients where tumor response was observed, half experienced a response of at least 4.2 months (95% confidence intervals: 3.0 months, 5.7 months)<sup>4</sup>

The second co-primary endpoint was 6 month progression-free survival (PFS); overall survival and safety were also evaluated

The median age of the patients treated with Avastin alone was 54 years. Additionally, 32 percent were female, 81 percent were in first relapse, 45 percent had a Karnofsky performance status (KPS) of 90 to 100 and 55 percent had a KPS of 70 to 80. Patients with active brain hemorrhage were excluded from the study.

Most adverse events related to Avastin in this trial appeared to be similar to those previously reported in

other studies of Avastin in other solid tumors. The most frequently reported adverse events in patients treated with Avastin alone were fatigue (45%), headache (37%), high blood pressure (30%), diarrhea (21%) and nose bleeds (19%). There were two deaths possibly associated with adverse events in the group of patients treated with Avastin alone.<sup>4</sup>

### **About Glioblastoma**

Glioma (cancer of the glial cells) is the most common type of malignant primary brain tumor (a tumor that originates in the brain), accounting for approximately one third of all cases diagnosed<sup>3</sup>. Glioblastoma (or glioblastoma multiforme; GBM) is the most common and most aggressive type of glioma<sup>3</sup>. The prognosis for patients with GBM is poor, and generally depends on the success of surgery to remove the tumor.

Glioblastoma affects approximately 10,000 people per year in the United States. Following initial treatment, glioblastoma tumors nearly always return and currently, there are limited treatment options for patients when these relapses occur. 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</sup>.

### **About Avastin**

Avastin is a biologic antibody designed to specifically inhibit the vascular endothelial growth factor (VEGF) protein that plays an important role in the development and maintenance of blood vessels, a process known as angiogenesis. VEGF is a potent activator of angiogenesis throughout the lifecycle of a tumor and is thought to be critical to a tumor's ability to grow and spread in the body (metastasize). Avastin is approved in EU for the treatment of the advanced stages of four common cancer types: colorectal cancer, breast cancer, lung cancer and kidney cancer. More than 500,000 patients have been treated with Avastin so far.

### **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).

All trademarks used or mentioned in this release are protected by law.

### **Roche Group Media Relations**

Phone: +41 -61 688 8888 / e-mail: [basel.mediaoffice@roche.com](mailto:basel.mediaoffice@roche.com)

- Daniel Piller (Head)
- Alexander Klauser
- Martina Rupp
- Claudia Schmitt
- Nina Schwab-Hautzinger

### **References**

1. Wong ET et al. J Clin Oncol 1999 ; 17 (8): 2572. Yung et al. Br J Ca 2000; 83: 588-93
2. Cloughesy T et al. Non-comparative Clinical Trial of Bevacizumab Alone or in Combination with CPT-11 Prolongs 6-Month Progression-free Survival in Recurrent, Treatment-Refractory Glioblastoma . Oral presentation # 2010b presented on Monday 2 June 2008 at ASCO
3. Central Brain Tumor Registry of the United States (CBTRUS). Primary Brain Tumors in the United States Statistical Report. Last accessed March 24 2009 at <http://www.cbtrus.org/reports/reports.html>
4. Avastin US Prescribing Information