Media release

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Innovative Roche cancer medicine Avastin approved in EU

First treatment of its kind with proven survival benefit for patients with advanced colorectal cancer

Roche today announced that the European Commission has approved Avastin (bevacizumab, rhuMAb-VEGF), the new innovative anti-angiogenesis drug for the treatment of patients with previously untreated metastatic colorectal cancer. Roche will now make Avastin available across Europe within the next few weeks and expects it to be accessible to physicians and patients early in the year.

Avastin is now approved for the first-line treatment of patients with metastatic carcinoma of the colon or rectum in combination with the chemotherapy regimens of intravenous 5-fluorouracil/folinic acid or intravenous 5-fluorouracil/folinic acid/Irinotecan.

"Today's full marketing approval represents a significant milestone for clinicians and patients across Europe engaged in the fight against cancer," said William M. Burns, CEO of Roche's Pharmaceuticals Division. "We will now work to ensure that this breakthrough treatment is widely available throughout Europe as quickly as possible."

"Avastin represents the culmination of decades of research looking into the process of angiogenesis," said Professor Eric Van Cutsem, University Hospital Gasthuisberg, Leuven, Belgium. "It is the first drug that works by choking off the blood supply that feeds tumours. Throughout several well designed clinical trials we have seen a meaningful increase in life expectancy when Avastin is combined with different chemotherapy regimens used in the treatment of advanced colorectal cancer."

The European Commission's approval was based on data from a landmark Phase III study published in *The New England Journal of Medicine* in June 2004 that showed patients treated with

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Avastin plus chemotherapy lived significantly longer than patients receiving chemotherapy alone, on average by nearly five months (20.3 months versus 15.6 months)[1]. Also, the addition of Avastin increased the amount of time that patients were without disease progression, on average four months, compared to patients receiving chemotherapy alone (10.6 months versus 6.2 months).

In 2000, colorectal cancer was the third most commonly reported cancer with 945,000 new cases worldwide.[2] It is estimated that over 50% of people diagnosed with colorectal cancer will die of the disease. In the European Union colorectal cancer is the second most common cause of death from any cancer in men.[3]

Roche and Genentech are pursuing a comprehensive clinical programme investigating the use of Avastin in advanced colorectal cancer with other chemotherapies and also expanding into the adjuvant setting (post operation). As Avastin's mechanism may be relevant in a number of malignant tumours, Roche and Genentech are also investigating the potential clinical benefit of Avastin in other cancers, including non-small cell lung cancer, pancreatic cancer, breast cancer and renal cell carcinoma. Approximately 15,000 patients are expected to be enrolled into clinical trials over the next years worldwide.

About Avastin

Avastin is the first treatment that inhibits angiogenesis – the growth of a network of blood vessels that supply nutrients and oxygen to cancerous tissues. Avastin targets a naturally occurring protein called VEGF (Vascular Endothelial Growth Factor), a key mediator of angiogenesis, thus choking off the blood supply that is essential for the growth of the tumour and its spread throughout the body (metastasis).

Avastin was approved in February 2004 in the US and has recently received full approval in Switzerland and Israel.

Roche in Oncology

Within the last five years the Roche Group, including its members Genentech in the United States and Chugai in Japan, has become the world's leading provider of anti-cancer treatments, supportive care products and diagnostics. Its oncology business includes an unprecedented five products with survival benefit in different major tumour indications: Xeloda and Herceptin in advanced stage breast cancer, MabThera in non-Hodgkin's lymphoma, Avastin in colorectal carcinoma and Tarceva in non-small cell lung cancer and pancreatic carcinoma.

In the United States Herceptin, MabThera, Avastin and Tarceva are marketed either by Genentech alone or together with its partners Biogen Idec Inc. (MabThera) and OSI (Tarceva). Outside of the United States, Roche and its Japanese partner Chugai are responsible for the marketing of these medicines.

The Roche oncology portfolio also includes NeoRecormon (anaemia in various cancer settings), Bondronat (prevention of skeletal events in breast cancer and bone metastases patients, hypercalcaemia of malignancy), Kytril (chemotherapy and radiotherapy-induced nausea and vomiting) and Roferon-A (hairy cell and chronic myeloid leukaemia, Kaposi's sarcoma, malignant melanoma, renal cell carcinoma). CERA is the most recent demonstration of Roche's commitment to anaemia management. The Roche Group's cancer medicines generated sales of more than 5.6 billion Swiss francs in the first nine months of 2004.

In addition to the medicines, Roche is developing new diagnostic tests that will have a significant impact on disease management for cancer patients in the future. With a broad portfolio of tumour markers for prostate, colorectal, liver, ovarian, breast, stomach, pancreas and lung cancer, as well as a range of molecular oncology tests, Roche will continue to be the leader in providing cancer-focused treatments and diagnostics.

Roche has four oncology research sites (two in the United States and one each in Germany and Japan) and five oncology development sites (two in the United States and one each in UK, Australia and Switzerland).

About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-intensive healthcare groups. Its core businesses are pharmaceuticals and diagnostics. As a supplier of innovative products and services for the prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is a world leader in diagnostics, the leading supplier of medicines for cancer and transplantation and a market leader in virology. In 2003, the Pharmaceuticals Division generated 19.8 billion Swiss francs in prescription drug sales, while the Diagnostics Division posted sales of 7.4 billion Swiss francs. Roche employs roughly 65,000 people in 150 countries and has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai.

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Further information:

About Roche: www.roche.com

About Genentech: www.gene.com

About cancer: www.health-kiosk.ch

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2. Ferlay, J, Bray,F, Pisani, P, and Parkin, D.M. GLOBOCAN 2000: Cancer Incidence, Mortality and Prevalence Worldwide, Version 1.0. IARC CancerBase No. 5. Lyon, IARCPress, 2001
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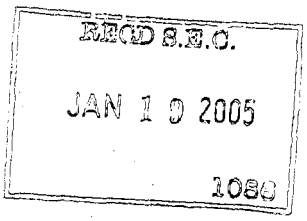

Basel, 12 January 2005

Roche's AmpliChip CYP450 Test receives FDA clearance

First microarray-based diagnostic test for detection of genetic variations that can influence drug efficacy and adverse drug reactions

Roche announced today that its first microarray-based test, the AmpliChip CYP450 Test, has been cleared by the US Food and Drug Administration (FDA) for diagnostic use in the United States. This test, which is powered by Affymetrix microarray technology, analyses a patient's Cytochrome P450 2D6 and 2C19 genotypes from genomic DNA extracted from a blood sample. Test results will allow physicians to consider unique genetic information from patients in selecting medications and doses of medications for a wide variety of common conditions such as cardiac diseases, pain and cancer.

"We are extremely pleased that the AmpliChip CYP450 Test has gained FDA clearance for use in this important market," said Heino von Prondzynski, CEO Division Roche Diagnostics and Member of the Roche Executive Committee. "This new tests allows physicians access to information that could help to prevent harmful drug interactions and to assure drugs are used optimally. Adverse drug reactions cause a huge number of hospitalizations in the US. Our new test also will, in some cases, enable patients to avoid suboptimal or even harmful treatment choices. For patients it is extremely important to know whether pain killers or anesthetics might work differently or not at all for them. Poor or slow metabolizers may experience much longer lasting effects of the treatment. The knowledge of the reasons behind this will empower people to ask for different and better-to-tolerate medicines. The use of this test is an important step forward in making personalized medicine a reality and has the potential to help physicians improve patient outcomes."

Two key genetic regions encoding the enzymes of the cytochrome P450 complex are the CYP2D6

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and CYP2C19 genes. The multiple variations in the CYP2D6 gene can result in poor, intermediate, extensive ("normal"), or ultra-rapid metabolism of CYP2D6-dependent drugs from a variety of classes, including anti-depressants, anti-psychotics, anti-arrhythmics, beta-blockers, pain medications, anti-emetics, and some anti-cancer drugs. Variations in the CYP2C19 gene result in either normal or poor metabolism of CYP2C19-dependent drugs from a variety of classes, including anti-convulsants, proton pump inhibitors, benzodiazepines, and anti-malarials.

Poor metabolizers treated with drugs that are dependent on "normal" enzyme activity are at increased risk for excessive or prolonged levels of the drug in their blood (excessive or prolonged therapeutic effect or toxicity), while ultra-rapid metabolizers may not achieve sufficient therapeutic levels in their blood with standard dosing. In the case of pro-drugs (that is, drugs that require enzymatic action before they become the therapeutic compound in the body), the opposite phenomenon occurs. It is important to note that multiple drugs taken at the same time (concurrent medications) and many other environmental factors such as diet, gender, and overall health, can inhibit or induce Cytochrome P450 enzyme activity.

The AmpliChip CYP450 Test was launched in Europe in the fall of 2004. The test combines the strengths of two industry gold-standards, Roche's patented polymerase chain reaction (PCR) amplification technology, which replicates even minute amounts of genetic material to detectable levels, and Affymetrix high-density microarray technology on glass chips no bigger than a thumbnail arrayed with tens of thousands of precisely arranged DNA fragments.

Affymetrix, Inc. announced on December 23rd, 2004 that its GeneChip System 3000Dx instrumentation, on which the AmpliChip CYP450 Test is run, has also received FDA clearance for diagnostic use in the United States.

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Additional information

- Roche Diagnostics: www.roche-diagnostics.com
- AmpliChip press kit: www.roche-diagnostics.com/press_lounge/amplichip_cyp450.html
- Affymetrix: www.affymetrix.com

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