# *Media Release*

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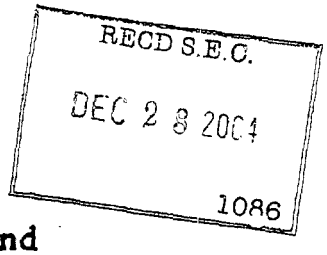


## Breakthrough cancer treatment Avastin approved in Switzerland

**First approval of innovative anti-angiogenesis medicine in Europe**

Roche today announced that the Swiss health authority Swissmedic has approved Avastin (bevacizumab, rhuMAb-VEGF) for the treatment of patients with previously untreated metastatic cancer of the colon or rectum. The Swiss approval lays the foundation for access to the medicine in more than 90 other countries. Roche will start to supply Avastin in Switzerland within the next few weeks and expects reimbursements to come through early next year.

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



"We were delighted when Swissmedic granted priority review to Avastin earlier this year, and now that the full marketing approval has been granted we will be working to ensure that Avastin is made available to cancer patients in Switzerland as quickly as possible," said William M. Burns, Head of Roche's Pharmaceuticals Division.

"The approval and availability of Avastin offers hope for patients with colorectal cancer, because it represents a major advance in the treatment of this disease. Avastin is the first drug that works by choking off the blood supply that feeds tumours," said Professor Richard Herrmann, Head of Oncology Department in the University Hospital Basel. "The significant increase in survival for patients provided by the addition of Avastin to a variety of different chemotherapy regimens used in the treatment of colorectal cancer, without the increase in side effects normally associated with chemotherapy, is a breakthrough in the treatment of this disease."

The approval is based on data from a landmark Phase III study published in the New England Journal of Medicine that showed patients treated with Avastin plus chemotherapy lived

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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] and 3,700 in Switzerland[3] respectively. It is estimated that over 50% of people diagnosed with colorectal cancer will die of the disease.

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, renal cell carcinoma and others. 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 of this year in the US and has recently received full approval in 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 research sites (two in the United States and one each in Germany and Japan) and five development sites (two in the United States and one each in UK, Australia and Switzerland).

**About Roche**

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**Further information:**

- www.roche.com
- www.gene.com
- www.health-kiosk.ch

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- Martina Rupp

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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
3. Vereinigung Schweizerischer Krebsregister, 2003

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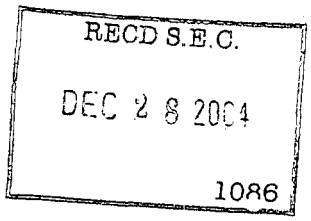


Basel, 20 December 2004

## Roche's new Invirase 500 mg receives approval in US after priority review by FDA

**Significant improvement of patient convenience by reducing pill count from 5 pills to 2 pills twice a day**

Roche's new Invirase 500 mg formulation has received U.S. Food and Drug Administration (FDA) marketing approval today following a six-month priority review process. The new 500 mg formulation will significantly reduce Invirase's pill count by more than half, from 5 to 2 pills twice a day. With less tablets per day, Invirase now becomes an excellent choice for HIV-patients who require treatment with an HIV-protease inhibitor.

"With the new Invirase 500 mg tablet now available, pill burden is considerably reduced and we anticipate that this improved convenience together with boosted Invirase's record of convincing data will result in an expansion of its use in the earlier stages of HIV therapy" said William M. Burns, Head of the Roche Pharmaceutical Division.

Invirase (saquinavir mesylate) is an HIV protease inhibitor approved for use in combination with a small dose of ritonavir ('boosting') and other anti-HIV medicines for the treatment of HIV infection. Boosted Invirase has been shown to be highly efficacious, with an excellent safety and tolerability profile and is recommended as first choice boosted protease inhibitor in the International AIDS Society (IAS) guidelines.

"The FDA approval of Invirase 500 mg together with the recently reported results of the Staccato trial is good news for patients as they now have access to a more convenient dosing regimen of a potent and well tolerated HIV drug" said Michael S. Saag, MD, Professor of Medicine and Director, UAB AIDS Outpatient Clinic, Birmingham, Alabama, USA. "In the Staccato trial patients treated with saquinavir/ritonavir showed one of the highest response rates in a clinical

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trial; after 24 weeks of treatment the HIV-virus was undetectable in around 90% of patients[1]."

**About Boosted Invirase**

Invirase, originally approved by the FDA in 1995, was the first HIV protease inhibitor on the market. Its introduction represented a major milestone in the treatment of HIV/AIDS. In December 2003, the FDA approved Invirase for use in boosted dosing regimens with ritonavir (1000 mg Invirase/100 mg ritonavir bid). Co-administering Invirase with ritonavir enhances therapeutic blood levels of the drug and enables simplified dosing.

Data from the Staccato clinical study show reductions in patients' HIV RNA recorded in the first 24 weeks on therapy that are the best ever seen in a large cohort of patients given HAART. Some 96% of patients achieved viral load reductions to <400 HIV RNA copies/ml and 91% were shown to have undetectable levels (<50 HIV RNA copies/ml). Over the 24 week induction phase of the study, these reductions in patient viral load were accompanied by a median increase of CD4 cells of 109 cells/mm$^3$.

**Roche in HIV**

Roche is at the forefront of efforts to combat HIV infection and AIDS, committed since 1986 to groundbreaking research and development of innovative new drugs and diagnostic technology. Invirase (saquinavir) was the first protease inhibitor (PI) and was introduced by Roche in 1995. Invirase/r (saquinavir 1000/ritonavir 100mg twice daily) has shown high efficacy, an excellent safety and tolerability profile and is recommended as first choice boosted protease inhibitor in the International AIDS Society (IAS) guidelines. Viracept (nelfinavir) has proven efficacy and safety in the treatment of HIV infection and has a unique cross-resistance profile, which is clinically proven to allow the future use of other drugs in its class. Viracept is supplied by Roche outside the USA, Canada, Japan and Korea.

Fuzeon received approval from the US Food and Drug Administration (FDA) in March 2003, from the European Commission and Switzerland in May 2003 and Canada in July 2003.

In addition, Roche successfully markets the AMPLICOR HIV-1 MONITOR TEST, version 1.5. This test from Roche Diagnostics is considered to be a highly sensitive measurement of the amount of HIV circulating in a patient's blood ("viral load"). With a limited number of treatment regimens available, the accurate monitoring of viral load levels is essential to establish and monitor the effectiveness of therapeutic regimens and assess the potential onset of drug resistance.

Roche is a committed partner of the Accelerating Access Initiative to increase access to HIV care in sub-Saharan Africa and the world's Least Developed Countries. For more information on

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[1] By an intent to treat analysis.

Roche policy and pricing of HIV protease inhibitors for these regions and research in HIV, visit www.roche-hiv.com/home/home.cfm

**About Roche**

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**Notes to Editors**

**References**

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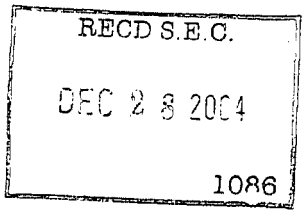


Basel, 22 December 2004

## Roche AIDS Walk: employees' initiative helps children affected by HIV/AIDS

**More than 1,1 million Swiss Francs raised for HIV/AIDS projects**

The "Roche AIDS Walk" mobilised 8000 employees around 60 sites on World AIDS day. Together, they walked or ran once around the world and thanks to their initiative, more than half a million Swiss Francs was raised. Roche doubled this amount, and 750 000 Swiss Francs will be donated to benefit orphans affected by HIV/AIDS in Malawi, Africa. Malawi is a stable and peaceful country but also one of the poorest in Africa, with up to half a million children who have lost one or both parents as a result of HIV/AIDS. The rest, 400 000 Swiss Francs, will go to local HIV/AIDS organizations in the participating countries.

Pierre Jaccoud, Chair of Roche's Corporate Sustainability Committee, said: "Roche concentrates its humanitarian aid efforts on developing and maintaining sustainable projects for people in the poorest countries of the world. We are happy to match the sum raised by the sponsors of the "Roche AIDS Walk" and to work in partnership with ECPP; together, we will ensure that our help will make a visible, long term and sustainable difference in the lives of the orphaned children.

**Support for HIV/AIDS projects in Malawi and beyond**

Supervised by the "European Coalition of Positive People", ECPP, the money will be used to build orphan centres and to purchase essential items, such as food, cooking utensils and clothes for the orphans in Malawi.

In addition to the money that will be used to help orphans in Malawi, 400 000 Swiss Francs raised at the Global Employee AIDS Walk will be donated to a local HIV/AIDS organization in many participating Roche affiliates and sites. As a result, children globally impacted by HIV/AIDS will benefit.

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**Partnership between Roche and ECPP**

Roche and ECPP have agreed to work in partnership to directly benefit orphaned children in Malawi and neighbouring Mozambique. The partnership is based on principles of transparency and trust to construct, equip and monitor orphan centres in these two regions. Roche commits to organise and bear all costs associated with hosting the Roche Employee AIDS Walk fundraising event and will assist ECPP with communications materials on the activities. Roche will also cover the administration cost of preparing the financial summary it requests from ECPP. In turn, ECPP will ensure that the orphans are the beneficiaries of the Roche Employee AIDS Walk funds. ECPP will also directly supervise the orphan centres in Malawi and Mozambique to ensure the resources reach and remain with the orphans. In addition, a quarterly update on progress and summary of how Roche Employee AIDS Walk funds have been utilised and expenditure planned will be created by ECPP. Any proposed changes to the scope of the project will be discussed between Roche and ECPP.

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**Further information:**

Roche AIDS Walk and Malawi:
www.roche.com/home/sustainability/sus_soc/sus_soc_coop/sus_soc_coop_vol.htm
Roche Pharmaceuticals in HIV: www.roche-hiv.com
Roche Diagnostics in HIV: www.roche-diagnostics.com/servicebox/document_center/index.php
Access to Healthcare: www.roche.com/home/sustain/sus_med.htm
About ECPP: www.ecpp.co.uk

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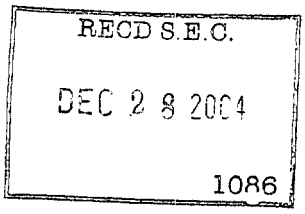


Basel, 22 December 2004

## Pegasys approved for chronic hepatitis B in Switzerland

Roche today announced that Pegasys (peginterferon alfa-2a (40KD)) has been granted marketing authorization by the Swiss regulatory authorities, Swissmedic, for the treatment of chronic hepatitis B. The approval has been granted for both the HBe antigen-positive and HBe antigen-negative forms of the disease and was based on one of the largest clinical development programmes in hepatitis B ever, which included three global studies in more than 1,500 patients.

The studies showed that Pegasys was superior to two therapies currently recommended first-line; interferon alfa and lamivudine. In contrast to lamivudine, the most commonly prescribed medication today, Pegasys works by a two-pronged approach. It stimulates the immune system as well as inhibits virus replication. This offers physicians a new option with the advantages of a finite treatment duration and lasting remission from the disease.

"This is a major milestone not only for Switzerland but for the more than 90 other countries worldwide that rely on Swiss regulatory review for their own approval process," said William M. Burns, Head of Roche's Pharmaceutical Division. "Based on the results of our clinical programme, we would anticipate that Pegasys will become a first-line treatment for chronic hepatitis B," he said, adding that Pegasys is the worldwide market leader for the treatment of hepatitis C.

**About chronic hepatitis B**

Chronic hepatitis B is a major global healthcare problem affecting more than 350 million people and it is one of the principal causes of liver failure, cirrhosis, and liver cancer. Between one-quarter and one-third of people with chronic hepatitis B will go on to develop progressive liver disease; and approximately one million die annually, making it the 10th leading cause of death worldwide.

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**Pegasys Superior to Standard Therapies**

Pegasys has been proven twice as effective as conventional interferon for the treatment of the most common form of chronic hepatitis B, hepatitis B e antigen (HBeAg) -positive chronic hepatitis B, in a multinational phase II trial. These findings were published in the July 2003 *Journal of Viral Hepatitis.*[1]

Two large-scale multinational phase III trials, in patients with both the HBeAg-positive and HBeAg-negative forms of chronic hepatitis B, demonstrated that after 48 weeks of therapy, more patients achieved a sustained response with Pegasys than with lamivudine. Furthermore, these studies demonstrated that the addition of lamivudine to Pegasys did not improve response rates over Pegasys alone.

The phase III study results in HBeAg-negative chronic hepatitis B, the most difficult-to-treat form of the disease, were published in September in the *New England Journal of Medicine,*[2] and the results of the phase III study in patients with HBeAg-positive chronic hepatitis B were presented at the 2004 Annual Meeting of the American Association for the Study of Liver Diseases in November.[3] Both lead investigators have stated that the results of these trials warrant Pegasys becoming the first-line treatment for HBeAg-positive or HBeAg-negative chronic hepatitis B.

"Until now, conventional interferon or lamivudine have been the first-line treatments for patients with chronic hepatitis B, but these clinical trials have proven that Pegasys outperforms both," said Dr George Lau, gastroenterologist at the Queen Mary Hospital, Hong Kong; and Assistant Dean in the Department of Medicine at the University of Hong Kong. "This approval means that we have a significant new option whereby patients can achieve a lasting remission and we only need to provide treatment for a limited 48-week period."

Pegasys was filed for the treatment of chronic hepatitis B simultaneously in Switzerland, the United States and the European Union in the summer of 2004, and approvals in the US and the EU are anticipated early in 2005. It is the first pegylated interferon indicated for the treatment of chronic hepatitis B anywhere in the world and has already been approved for this indication in Thailand and Taiwan.

**About Pegasys**

Pegasys, a new generation hepatitis therapy that is different by design, has already become the worldwide market leader in hepatitis C. Pegasys has a dual immunomodulatory and antiviral mode of action. The improved pharmacokinetic profile ensures drug plasma concentrations are maintained at constant levels throughout the one week dosing interval. Pegasys therapy in chronic hepatitis B is given once weekly as a 180 µg subcutaneous injection for a 48-week period.

**Roche in hepatitis**

Roche is committed to the viral hepatitis disease area, having introduced Roferon-A for hepatitis B and C, followed by Pegasys in hepatitis C and a full development program in hepatitis B. Roche has its own brand of ribavirin, Copegus, which is used in conjunction with Roferon A or Pegasys for HCV. In addition, Roche manufactures HBV and HCV diagnostic and monitoring systems: The COBAS AMPLICOR Test, and the AMPLICOR MONITOR Test, two testing systems used to detect the presence of, and quantity of, HBV DNA or HCV RNA in a person's blood. Roche has just received a positive opinion from the EMEA in the European Union for a new indication for Pegasys and Copegus as a treatment for patients co-infected with HIV and HCV. More than 40,000 patients worldwide continue to participate in trials with Pegasys and Copegus as Roche examines the unmet medical needs of hepatitis C patients. Roche's commitment to viral hepatitis also extends to its pursuit of strategic alliances and partnerships to develop new compounds for the future.

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**Further information:**

WHO Hepatitis B fact sheet: www.who.int/mediacentre/factsheets/fs204/en (English)

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