Investor Update

Tuesday, June 22, 2004 8:02 AM

Roche submits application to U.S. FDA for new formulation of Invirase
-- new 500 mg tablet to simplify dosing regimens
-- filing in Europe to follow within days

Roche today announced the submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for approval to market a new 500 mg tablet formulation of its HIV protease inhibitor Invirase (saquinavir mesylate). The new formulation of Invirase is smaller in size than the currently available 200 mg Invirase capsule and, if approved, will reduce pill count for each dose by more than half (from five pills to two, twice-daily). A filing for approval to market the new formulation in the European Union (EU) will be submitted to the European Medicines Agency (EMEA) within days of the U.S. filing.

The U.S. FDA approved Invirase 1000 mg for use in combination with ritonavir 100 mg and other anti-HIV drugs in December 2003. Co-administering Invirase with ritonavir provides therapeutic blood levels of the drug and enables simplified, twice-daily dosing. Today's filing is based on a bioequivalence study demonstrating that two 500 mg tablets of Invirase, together with 100 mg of ritonavir, achieve similar levels of Invirase in the blood as five Invirase 200 mg capsules with 100 mg ritonavir.

"It is important to develop anti-HIV therapies that are not only potent and well-tolerated but will also improve convenience for patients, which can help to maximize adherence to a treatment regimen," said Nicholas Bellos, M.D., President, Southwest Infectious Disease Associates, Dallas, Texas.

"The 500 mg tablet is another important example of Roche's commitment to the treatment of HIV and to the continued optimization of dosing for Invirase. If approved, it will offer patients a smaller pill and the ability to take a full dose with fewer pills," said Max Bucher, Global Head of Hospital Care Business, Roche. "We will extend our commitment to Invirase through a comprehensive clinical program that will further explore its role in the treatment of HIV."

References

1. Dragsted UB, Gerstoft J, Pedersen C et al. JID. 2003:188:635-642. [MaxCmin 1 trial]
2. Youle M, Gerstoft J, Fox Z et al. 2nd IAS. Paris, France, 2003; Poster LB23. [MaxCmin 2 trial]

Notes to editors:
MaxCmin 1 and MaxCmin 2 trials
Head-to-head trials of boosted protease inhibitors. In the trials saquinavir/r 1000/100 mg bid outperformed indinavir/r 800/100 mg bid in efficacy and showed comparable antiviral potency to lopinavir/r 400/100 mg bid.

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) has shown high efficacy, an excellent safety and tolerability profile and is recommended in the new antiretroviral WHO guidelines. Invirase is used in double boosting, a new treatment trend which combines two PIs with a minidose ritonavir. Viracept (nelfinavir) has proven efficacy and safety in the treatment of HIV infection and is widely used as a first line early treatment. It has a unique cross-resistance profile, which is clinically proven to allow the future use of other drugs in its class. Roche

Viracept 625mg provides reduced pill count and improved GI tolerability and received approval in Europe in May 2004. 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, and 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 Roche policy and pricing of HIV protease inhibitors for these regions and research in HIV, visit www.roche-hiv.com.

About Roche
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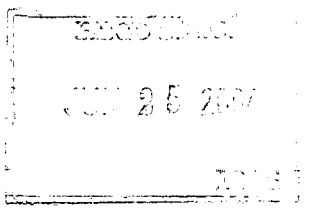

Basel, 22 June 2004

European Commission approves Herceptin plus Taxotere as first-line therapy in HER2-positive metastatic breast cancer

Life-extending combination offers new hope to patients across Europe

Roche announced today that the European Commission has approved the use of Herceptin (trastuzumab) in combination with Taxotere (docetaxel) in the European Union as a first-line therapy in HER2-positive metastatic breast cancer patients who have not yet received chemotherapy for their disease. HER2-positive breast cancer patients suffer from a particularly aggressive form of breast cancer which traditionally has a poor prognosis.

The approval is based on study results[1] which showed that for women with HER2-positive breast cancer, the combination of Herceptin and Taxotere significantly improved median life expectancy by more than one-third (31 months with Herceptin plus Taxotere vs. 22 months for Taxotere alone). The study also showed that 61% of patients treated with the combination responded to treatment, compared to 34% of patients who received Taxotere alone.

"The early use of this new combination therapy represents a vital life-extending treatment option for patients, and highlights the critical importance of verifying HER2 status upon diagnosis of breast cancer," said William M. Burns, Head of Roche's Pharmaceuticals Division. "Now that this combination therapy will be made available to women across Europe, this further consolidates the position of Herceptin as the foundation of care in HER2-positive metastatic breast cancer."

In an earlier trial, Herceptin also showed a survival benefit when used as a first-line therapy in combination with Taxol (paclitaxel). Both Taxol and Taxotere belong to the most commonly used

[1] M77001 12-month update results, presented at the European Breast Cancer Conference in March 2004

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class of chemotherapy agents for metastatic breast cancer in Europe, known as 'taxanes'. This trial with Herceptin and Taxotere firmly establishes Herceptin in combination with taxanes as the foundation of care for women with HER2-positive metastatic breast cancer.

The aggressive nature of HER2-positive breast cancer makes both the survival and response rates highly meaningful. In HER2-positive breast cancer, increased quantities of the HER2 (Human Epidermal growth factor Receptor 2) protein are present on the surface of the tumour cells. This is known as 'HER2 overexpression'. High levels of HER2 overexpression are present in a particularly aggressive form of the disease which responds poorly to chemotherapy. Research shows that HER2 overexpression affects approximately 20-30% of women with breast cancer.

About the study

188 patients were recruited into the study (M77001), 94 patients randomised to receive Herceptin plus Taxotere and 94 randomised to receive Taxotere alone. Two patients in the combination arm did not receive study drug and were excluded from the final analysis. Taxotere was scheduled at a dose of 100 mg/m2 every 3 weeks for at least 6 cycles. Herceptin was administered in 2mg/kg weekly doses until disease progression (after an initial loading dose of 4mg/kg). Patients in the Taxotere arm of the study were given the option to cross over to receive Herceptin, following disease progression.

About breast cancer and Herceptin

Eight to nine percent of women will develop breast cancer during their lifetime, making it one of the most common types of cancer in women.[2] Each year more than one million new cases of breast cancer are diagnosed worldwide, with a death rate of nearly 400,000 people per year.

Herceptin is a targeted humanised antibody treatment that received approval in the European Union in 2000 for use in patients with metastatic breast cancer, whose tumours overexpress the HER2 protein. In addition to being indicated for use in combination with Taxotere as a first-line therapy in HER2-positive patients who have not received chemotherapy for their metastatic disease, it is also indicated as a first-line therapy in combination with Taxol, and as a single agent in second- and third-line therapy. Herceptin is marketed in the United States by Genentech, in Japan by Chugai and internationally by Roche.

[2] World Health Organisation, 2000

Roche in Oncology

Within the last five years the Roche Group including its partners Genentech in the US 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 four marketed products with survival benefit in different major tumour indications: Xeloda and Herceptin in advanced stage breast cancer, MabThera in non-Hodgkin's Lymphoma, and Avastin in Colorectal Carcinoma. In the United States Herceptin and Avastin are marketed by Genentech alone and MabThera/Rituxan by Genentech together with Biogen Idec Inc. Outside of the United States, Roche and its Japanese partner Chugai are responsible for the marketing of these drugs.

The Roche oncology portfolio also includes NeoRecormon (anaemia in various cancer settings), Bondronat (prevention of skeletal events in breast cancer and bone metastases patients, hypercalcemia 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 the commitment to anaemia management. The Roche Group's cancer medicines generated sales of more than 6 billion Swiss francs in 2003.

In a recent phase III study Tarceva met its primary endpoint of improving overall survival in patients with non-small cell lung cancer. Tarceva is being developed by Roche, Genentech and OSI Pharmaceuticals. Chugai is pursuing its development and regulatory approval for the Japanese market.

Roche is developing new tests, which 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, we will continue to be the leaders in providing cancer focused treatments and diagnostics.

Roche Oncology has four research sites (two in the US, Germany and Japan) and four Headquarter Development sites (two in the US, UK and Switzerland).

About Roche

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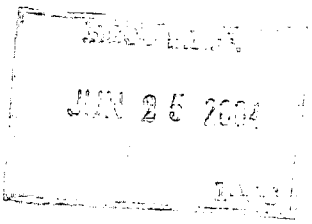
and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche employs roughly 65,000 people in 150 countries. The Group has alliances and research and development agreements with numerous partners, including majority ownership interests in Genentech and Chugai.

Further information:

Herceptin: www.HER2status.com and www.heratrial.com

Cancer disease: www.health-kiosk.ch

Media release



Basel, 23 June 2004

Roche to strengthen global leadership in biotechnology manufacturing

New production facilities planned at Group's Basel and Penzberg sites

To enable it to continue to meet steadily growing demand for its innovative new medicines, the Roche Group intends to expand its manufacturing capacity for biotechnology products. The company plans to construct a new biotech centre at the Group's Basel campus and an additional facility at the Penzberg site in Germany. The projects, representing capital expenditures of about 400 million Swiss francs each, will take three years to complete. The new facilities will initially be used to manufacture the active ingredients of the anti-cancer medicines Avastin and Herceptin, both of which belong to a group of therapeutic agents known as monoclonal antibodies. To operate the new Basel and Penzberg facilities, Roche will be creating roughly 150 new jobs at each site.

'This investment underscores our intention of ranking among the world's top biotechnology companies in every area, from research and development to production and marketing', says Roche Chairman and CEO Franz B. Humer. 'Biopharmaceuticals have led to therapeutic breakthroughs in a number of disease areas, notably oncology. By expanding our manufacturing facilities, we are also taking steps to ensure that we can continue to supply these medicines to all patients who need them. Further more, these milestone projects are a clear expression of our ongoing commitment to our large and important sites in Basel and Penzberg.'

At Group headquarters in Basel an existing chemical production building will be torn down to make room for a new eight-storey biotech centre designed by the architectural firm of Herzog & de Meuron. In Penzberg, the largest biotechnology manufacturing site in Europe, existing capacity will be expanded by adding a new five-storey facility.

Today, Roche already has the world's largest manufacturing capacity for biopharmaceuticals. Apart from Basel and Penzberg, the Group has biopharmaceutical production facilities in Nutley (USA);

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at the Genentech sites in Vacaville (USA), Porriño (Spain) and South San Francisco (USA); and at the Chugai sites in Utsunomiya and Ukima (both in Japan).

About Avastin

Avastin (bevaciszumab), a therapeutic antibody manufactured using recombinant DNA technology, is the first medicine for metastatic colorectal cancer to be based on a completely new approach known as anti-angiogenesis. The medicine selectively inhibits vascular endothelial growth factor (VEGF), which plays a critical role in the formation and growth of new blood vessels (angiogenesis). By reducing tumour angiogenesis, Avastin inhibits the growth and spread of cancers. Avastin received FDA approval for the US market early this year, and Roche is currently working closely with European regulators to ensure that the product is available to patients in Europe as soon as possible.

About Herceptin

Herceptin (trastuzumab) is a therapeutic antibody manufactured using recombinant DNA technology, and it is the first oncogene-targeting medicine shown to provide a survival benefit in breast cancer. The product is designed to specifically target the HER2 gene, which is associated with aggressive cancer cell growth. Unlike chemotherapeutic agents, Herceptin does not destroy normal, healthy cells. Destruction of healthy cells is the primary cause of unwanted side-effects in patients receiving conventional cancer treatments.

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Additional information

- Fact sheet on the new biotechnology facility in Basel (in German only):
  www.roche.com/pages/downloads/company/pdf/040623fsbs.pdf
- Picture on the new biotechnology facility in Basel:
  www.roche.com/pages/downloads/company/pdf/040623ansbs.pdf
- Fact sheet on the new biotechnology facility in Penzberg (in German only):

www.roche.com/pages/downloads/company/pdf/040623fspen.pdf

- Picture on the new biotechnology facility in Penzberg:

www.roche.com/pages/downloads/company/pdf/040623anspen.pdf

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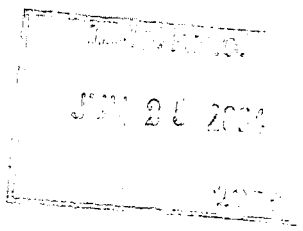

Investor Update

June 23, 2004 7:47 AM

Roche and Kosan announce indication changes for KOS-862 phase II trials

Roche and Kosan Biosciences Incorporated today announced plans to initiate a phase II trial of KOS-862 (R1492) in prostate cancer, while terminating a phase II trial in colorectal cancer. Prostate cancer has been selected for further clinical development because of the high response rates recently reported for the epothilone class of drugs in this indication. The KOS-862 trial in colorectal cancer will be terminated due to unanticipated cumulative drug toxicities in patients who had been previously treated with oxaliplatin. A planned phase Ib combination trial of KOS-862 with Xeloda to support the colorectal trial will not be initiated.

Roche and Kosan entered into an alliance for the co-development of KOS-862 and its back up compounds in September 2002. The partners expect to file an IND application and initiate a phase I clinical trial for a second epothilone compound in 2004. Currently, Roche and Kosan are discussing extending their relationship to generate and develop additional epothilone drug candidates.

"Although we have concluded the colorectal cancer trials, the response rate of patients with prostate cancer towards other epothilones leads us to be optimistic about the potential efficacy of KOS-862 in this type of tumor," said Daniel V. Santi, M.D., Ph.D, Chairman and Chief Executive Officer of Kosan.

William M. Burns, Head of Roche's Pharmaceuticals Division, added, "Roche is confident in the potential of epothilones as important anticancer agents. We are pleased that the Roche-Kosan collaboration continues to move KOS-862 through the appropriate efficacy trials, while advancing next-generation epothilone analogs through the pipeline."

About Kosan
Kosan Biosciences has two lead product candidates: KOS-862 and 17-AAG, including its proprietary formulation designated KOS-953. Both compounds are derived from an important class of natural products known as polyketides. KOS-862 is currently in Phase II trials in non-small cell lung and breast cancers; it is partnered with Roche in a global development and commercialization agreement. 17-AAG is being evaluated in multiple Phase I and Phase Ib clinical trials in collaboration with the National Cancer Institute. By applying its expertise and proprietary technologies to generate polyketide analogs and by increasing the production yields of polyketides, Kosan has created a robust pipeline of potentially significant products for cancer, as well as for infectious disease and other therapeutic areas. For additional information on Kosan Biosciences, please visit the Company's website at www.kosan.com.

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