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ROCHE HOLDING 82-3315

[Translation of a German Advertising, published in the "SHAB Schweizerisches Handelsamtsblatt" (Swiss Official Gazette of Commerce) on April 8, 2004]

Roche Holding Ltd

Roche Holding Ltd is a publicly listed company on the Swiss Stock Exchange. The company has a share capital of CHF 160 million, divided into 160,000,000 fully paid bearer shares with a nominal value of CHF 1 each. In addition, the company has issued 702,562,700 non-voting equity securities (*Genussscheine*) to bearer. The company is based in Basel and has its registered office at Grenzacherstrasse 124, 4070 Basel.

Pursuant to Art. 20 of the Swiss Stock Exchange Act, notification has been given by a contractually constituted group of shareholders of a change in the composition of the group. Following the departure, effective 6 April 2004, of Dr Fritz Gerber from this group of shareholders with pooled voting rights, the group will continue to exist with its remaining members and will continue to hold a combined total of 80,020,000 bearer shares (50.01% of the voting stock). The remaining members of this group of shareholders are:

Dr Lukas Hoffmann
Mrs Vera Michalski-Hoffmann
Mrs Maja Hoffmann
Mr André S. Hoffmann
Dr Andreas Oeri
Mrs Sabine Duschmalé-Oeri
Mrs Catherine Oeri
Mrs Beatrice Oeri
Mrs Maja Oeri

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Media release

Roche

Basel, 26 April 2004

R1549 does not meet primary endpoint in phase III study in ovarian cancer

Roche and Antisoma announced today that they have completed SMART (Study of Monoclonal Antibody RadioimmunoTherapy), a phase III study of R1549 in ovarian cancer. The outcomes for R1549-treated patients appeared no better than those of patients in the comparative arm of the trial. Given these findings, it is unlikely that development of R1549 will continue. A more detailed analysis of the data from SMART will be completed. The trial provides an extensive clinical database which may be of interest for future research into ovarian cancer.

William M. Burns, Head of Roche's Pharmaceuticals Division, said "Drug development is a high-risk endeavour and such results are not unexpected in the development of novel treatment modalities. The outcome of this study will have no impact on our growth outlook and we remain committed to our long-term relationship with Antisoma, which is based upon multiple products. Commercially more important, Roche also announced today highly significant phase III data on Tarceva in non-small cell lung cancer which will be the next regulatory submission of a major product contribution to the treatment of cancer. The Roche group will be in the unparalleled position of having five cancer medicines with a proven survival benefit - Herceptin, MabThera, Xeloda, most recently Avastin and now Tarceva."

Commenting on the result, Glyn Edwards, CEO of Antisoma said "We're obviously disappointed by the R1549 result, but will now have the opportunity to focus all our efforts on the strong, diverse and rapidly advancing pipeline of other drugs we have in development. We're also confident that we will add further to our clinical portfolio by the end of this year.'

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Antisoma and Roche are co-developing a number of drugs under the broad strategic alliance formed in November 2002. These include R1550, a humanised monoclonal antibody in phase I trials for breast cancer, and AS1404, a small-molecule vascular targeting agent, that is expected to start a phase II programme of combination studies later this year.

About the SMART study

SMART (Study of Monoclonal Antibody RadioimmunoTherapy) is a phase III randomised, single-blinded parallel group trial that began in 1998. The trial included more than 420 women with ovarian cancer in seventeen countries and compares patients who received standard care plus R1549 with patients who received standard care alone. Women receiving R1549 were given a single dose of the drug via a catheter into the abdomen (intraperitoneal administration) after surgery and chemotherapy.

R1549

R1549 is a monoclonal antibody linked to the radioactive isotope yttrium-90 using a chelating agent (linker) CITC-DTPA. The antibody component binds to a protein (MUC1) found on the surface of ovarian cancer cells.R1549 was originally developed at the Imperial Cancer Research Fund (now Cancer Research UK) in London. Antisoma licensed the drug from Imperial Cancer Research Technologies (now Cancer Research Technologies) in 1996.

Roche – Antisoma Collaboration

In November 2002, Roche and Antisoma entered into an expansive alliance to provide Roche with access to Antisoma's broad portfolio of oncology compounds. To date, two compounds have been incorporated into Roche's clinical portfolio (R1549 and R1550 – a humanized monoclonal antibody targeting MUC1). Additionally, Roche maintains the option, effective for the first five years of the collaboration, to license any of Antisoma's preclinical oncology compounds when they start clinical trials. Roche currently holds a minority equity stake in Antisoma.

Roche in Oncology

Within the last five years the Roche Group 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: Herceptin, MabThera, Xeloda and Avastin which has been launched in the US recently, treat a range of malignancies such as breast cancer, non-Hodgkin's lymphoma and colorectal cancer. Other key products include 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 (leukaemia, Kaposi's sarcoma, malignant melanoma, renal cell carcinoma). Roche's cancer medicines generated sales of more than 6 billion Swiss francs in 2003.

Based on a positive phase III study Tarceva, the first and only EGFR-targeted drug, showed improved survival in patients with non-small cell lung cancer.

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

Headquartered in Basel, Switzerland, Roche is one of the world's leading innovation-driven healthcare groups. Its core businesses are pharmaceuticals and diagnostics. Roche is number one in the global diagnostics market, the leading supplier of pharmaceuticals for cancer and a leader in virology and transplantation. As a supplier of 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 employs roughly 62,000 people in 150 countries. The Group has alliances and research and development agreements with numerous partners, including majority ownership interests in Genentech and Chugai.

About Antisoma

Based in London, UK, Antisoma is a biopharmaceutical company that develops novel products for the treatment of cancer. The Company fills its development pipeline by acquiring promising new product candidates from internationally recognised academic or cancer research institutions. Its core activity is the pre-clinical and clinical development of these drug candidates. Antisoma forms partnerships with pharmaceutical companies to bring its products to market. Visit www.antisoma.com for further information about Antisoma.

Media Release

Roche

Basel, 26 April 2004

New cancer drug Tarceva – a breakthrough with significant survival benefit in patients with advanced lung cancer

First and only drug in a new class (HER1/EGFR-inhibitors) to show survival benefit in a randomized phase III trial

Roche, Genentech, Inc. and OSI Pharmaceuticals, Inc., today announced positive results from a phase III study of Tarceva (erlotinib) in relapsed non-small cell lung cancer (NSCLC) patients. The study met its primary endpoint of improving overall survival with patients on Tarceva living longer than those in the placebo arm. The trial also met secondary endpoints including improving time to symptomatic deterioration, progression-free survival and response rate.

"These Tarceva results are great news, confirming the earlier promising single agent activity in patients with relapsed non-small cell lung cancer. Tarceva is the first and only EGFR-targeted drug showing improved survival in patients with NSCLC. We will be striving to make Tarceva available as quickly as possible to patients," said William M. Burns, Head of Roche's Pharmaceuticals Division. "Tarceva joins Herceptin, MabThera, Xeloda and Avastin as the fifth cancer medicine in our portfolio with a proven survival benefit. This puts us in an unparalleled position and further underlines Roche's leadership in oncology."

"Tarceva is the first EGFR-inhibitor that has been shown to extend survival in patients with relapsed non-small cell lung cancer, for whom there are very limited treatments possible," said Professor Nick Thatcher, Chairman on Lung Cancer Group, Christie and Wythenshawe Hospitals Manchester, UK. "The results of this controlled trial with Tarceva are very exciting for all of us in the oncology community. But even more so for people with lung cancer, the biggest cancer killer in Europe."

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About the Study

The international study was conducted by the National Cancer Institute of Canada, Clinical Trials Group at Queens University (NCIC CTG) in collaboration with OSI. The primary endpoint in this study was overall survival. Secondary endpoints include time to symptomatic deterioration, progression-free survival, safety, and tumour response.

The alliance of Roche, OSI and Genentech will work with the NCIC CTG to submit data from this phase III trial for presentation at the upcoming 2004 Annual Meeting of the American Society of Clinical Oncology (ASCO) in New Orleans from June 5 – 8.

About Tarceva

Tarceva is a small molecule designed to target the human epidermal growth factor receptor 1 (HER1) pathway, which is one of the factors critical to cell growth in many cancers. HER1, also known as EGFR, is a key component of the HER signalling pathway, which plays a role in the formation and growth of numerous cancers. Tarceva is designed to inhibit the tyrosine kinase activity of the HER1 signalling pathway inside the cell, which may block tumour cell growth. Results of a phase III trial of Tarceva in pancreatic cancer are expected in the second half of 2004. Early-stage trials of Tarceva are being conducted in other solid tumours, such as ovarian, colorectal, head and neck, renal cell carcinoma, glioma and gastrointestinal cancers.

About Non-Small Cell Lung Cancer

According to the World Health Organization, there are more than 1.2 million cases worldwide of lung and bronchial cancer each year, causing approximately 1.1 million deaths annually. Non-small cell lung cancer is the most common form of the disease and accounts for almost 80 percent of all lung cancer.

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Genentech is a leading biotechnology company that discovers, develops, manufactures and commercialises biotherapeutics for significant unmet medical needs. Eighteen of the currently approved biotechnology products originated from, or are based on, Genentech science. Genentech manufactures and commercialises 13 biotechnology products in the United States. The company has headquarters in South San Francisco, California, and is traded on the New York Stock Exchange under the symbol DNA.

OSI Pharmaceuticals is a leading biotechnology company focused on the discovery, development, and commercialisation of high-quality, next-generation oncology products that both extend life and improve the quality of life for cancer patients worldwide. OSI has a balanced pipeline of oncology drug candidates that includes both novel mechanism-based, gene-targeted therapies focused in the areas of signal transduction and apoptosis and next-generation cytotoxic chemotherapy agents. OSI has a commercial presence in the U.S. oncology market where it exclusively markets Novantrone (mitoxantrone concentrate for injection) for approved oncology indications and Gelclair for the relief of pain associated with oral mucositis.

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Further Information:

www.roche.com

www.gene.com

www.osip.com

Roche

Investor Update

April 26, 2004

CellCept was associated with reduced incidence of cancer, compared to Azathioprine, following heart transplant

A study presented today at an international transplant meeting showed that heart transplant patients treated with the immunosuppressant CellCept (mycophenolate mofetil) in standard immunosuppressive regimens had a significantly lower risk of developing cancer compared to those receiving non-CellCept-based treatment regimens. Presented at the annual meeting of the International Society for Heart and Lung Transplantation (ISHLT), the study found a 27% lower risk of cancer in CellCept-treated patients. Patients studied were part of the ISHLT Transplant Registry.

"Though not derived from randomized controlled trials, these data indicate that the choice of maintenance immunosuppressive regimen may be a modifiable risk factor for the development of malignancy in heart transplant recipients," said James O'Neill, M.D., Fellow in Heart Failure and Cardiac Transplantation, Cleveland Clinic.

Previous research had shown that organ transplant recipients receiving immunosuppressive therapy are three to four times more likely to develop tumors than the general population and have an even greater risk of developing certain rare cancers.*

Extensive examination of registry validates CellCept treatment
The study, Mycophenolate Mofetil and the Risk of Developing Malignancy Following Orthotopic Heart Transplantation (OHT), examined competing risk factors to determine which are associated with malignancy following OHT, and was based on 3,895 patients in the ISHLT Transplant Registry. The study examined survival without malignancy in patients taking standard immunosuppressive regimens (defined as cyclosporine or tacrolimus and azathioprine or CellCept), who underwent OHT between January 1, 1995, and December 31, 1997.

Of these patients, 703 (18%) developed malignancy during the follow-up period through June 30, 2002. The breakdown of malignancy was as follows: skin (47%), post-transplant lymphoproliferative disease (10%), other malignancies (33%), unreported (10%).

Independent predictors of significantly increased risk were a pre-transplant history of cancer and increased age, while the use of CellCept was significantly protective (27% lower relative risk; 95% confidence interval: 0.56-0.95; P-value: 0.02). Relative to the mean age of 55 years, the risk of malignancy for 30, 45 and 60 years of age was 0.32, 0.46 and 1.37 respectively. Female gender was associated with a 32% reduced relative risk. Neither OKT3 nor ATG use was associated with an increased risk of malignancy. These findings build on the results from two studies presented at last year's American Transplant Congress, in which kidney transplant patients treated with CellCept were not significantly more likely to develop lymphoma/post-transplant lymphoproliferative disorder (PTLD) than those patients who were not exposed to the drug.

"Data such as these are critical to increasing our understanding of the risks that follow organ transplantation," said Dr. O'Neill. "The better we can manage those risks, the better the patient's long-term prognosis."

About CellCept
CellCept is an immunosuppressant or anti-rejection drug used in combination with other immunosuppressive drugs (cyclosporine and corticosteroids) for the prevention of rejection in patients receiving heart, kidney and liver transplants. CellCept received FDA approval for the prevention of organ rejection in kidney (May 1995), heart (February 1998), and liver (July 2000). The recommended dosages for CellCept follow: for adult kidney transplants, 2 g daily; for pediatric kidney transplants, oral suspension 600 mg/m2; for adult heart and liver, 3 g/day.

The principal adverse events associated with the administration of CellCept (in combination with cyclosporine and corticosteroids) include diarrhea, leukopenia, sepsis and vomiting, and there is evidence of a higher frequency of certain types of infections. A higher proportion of renal transplant patients in the active treatment groups experienced one or more opportunistic infections compared with patients receiving placebo. Cytomegalovirus tissue invasive disease was more common in patients receiving 3 g/day.

Increased susceptibility to infection and the possible development of lymphoma and other malignancies, particularly of the skin, may result from immunosuppression. Only physicians experienced in immunosuppressive therapy and management of renal, cardiac or hepatic transplant patients should use CellCept. Patients receiving the drug should be managed in facilities equipped and staffed with adequate laboratory and supportive medical resources. The physician responsible for maintenance therapy should have complete information requisite for the follow-up of the patient.

There are no adequate and well-controlled studies in pregnant women. However, CellCept has been shown to have teratogenic effects in animals; it may cause fetal harm when administered to a pregnant woman. Therefore, CellCept should not be used in pregnant women unless the potential benefit justifies the potential risk to the fetus.

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* Penn I. Post-transplant malignancy: the role of immunosuppression. Drug Safety Aug 2000; 23(2), 101-13

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