

# Investor Update

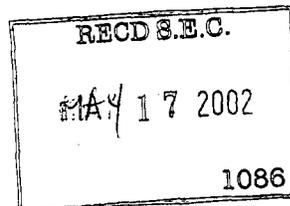
Roche



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Basel, 14 May 2002

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**New exciting data shows ibandronate (Bonviva) is highly effective and well tolerated in postmenopausal women with osteoporosis**  
First osteoporosis medication to show fracture reduction with a between dose interval of >2 months

Ibandronate, a potent new bisphosphonate being developed by Roche/GSK, was shown to significantly reduce fractures in women with post menopausal osteoporosis, according to data presented at the 2002 World Congress of Osteoporosis in Lisbon.

The data showed that for the first time a bisphosphonate reduces fractures even when patients have a drug free period of up to two months in every quarter. Oral ibandronate (taken daily or at regular intervals followed by a between dose period) was highly effective in reducing the risk of vertebral fractures and was simple to use and well tolerated, all of which could lead to greater patient compliance, which can be a problem with other medicines.

Further data presented also showed intravenous ibandronate significantly increased lumbar spine bone mass density, underlining this as a promising alternative route of administration for certain patients who seek the simplicity and freedom from regular oral dosing.

"These exciting new results show that ibandronate provides an effective therapy for the management of osteoporosis and will enhance patient's compliance. Based on the potency of the drug and on the promising results obtained so far Roche/GSK have further studies ongoing with a number of novel oral and intravenous treatment regimens. Ibandronate will enable Roche/GSK to become a key player in the osteoporosis market." says Philippe Van der Auwera, Life Cycle Leader Ibandronate at Roche.

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### **About ibandronate**

Ibandronate, a highly potent nitrogen-containing bisphosphonate, is currently in Phase II/III clinical development, for the treatment and prevention of postmenopausal osteoporosis. It has been studied to date in clinical trials involving over 9000 patients. In order to bring to market a drug with innovative benefits to physicians and patients, a further clinical development programme is evaluating monthly oral and quarterly intravenous dosage regimens in women with postmenopausal osteoporosis.

### **Osteoporosis**

Osteoporosis is a disease characterised by low bone mass and fragility and a consequent increase in fracture risk and disability. It is estimated that 1 out of 3 postmenopausal women aged 50 years and older is affected by osteoporosis. One in two women over the age of 50 will have an osteoporosis-related fracture in their lifetime. Approximately 80% of osteoporosis occurs in women, 20% in men.

### **About the Studies**

#### **Oral Study**

Data from the three year oral study were presented by Professor Pierre Delmas, President of the International Osteoporosis Foundation. 2,946 post menopausal women aged between 55 and 80 years at risk of osteoporosis were treated with either placebo or one of two ibandronate schedules: daily oral ibandronate (2.5mg) or oral ibandronate (20mg) on alternate days for 12 doses at the beginning of every three month cycle. The primary endpoint of the study was the risk or incidence of vertebral fracture (VF) after three years. The results indicated that both daily and intermittent oral ibandronate significantly reduced the risk of radiological confirmed VF by 62% and 50% respectively compared to placebo. Ibandronate demonstrates the numerically highest reduction in risk of vertebral fractures of all bisphosphonates.

#### **Intravenous Study**

The intravenous study data were presented by Professor Adami, Professor of Medicine, University of Verona, Italy. The trial recruited 520 post-menopausal women aged between 55 and 75 years selected for their low score of BMD (bone mineral density). Patients received intravenous ibandronate 1mg or 2mg or placebo as a 3-monthly bolus injection. The endpoint of the study was the relative change in BMD of the lumbar spine. After one year, 2mg intravenous ibandronate increased lumbar spine BMD by 5% compared to 3% with 1mg intravenous ibandronate and 0.3% with placebo. In addition, ibandronate produced significant suppression of bone markers

(indicators of bone turnover). Tolerability was very good. These data underpin the promise of intravenous regimens that, given as a simple 4 times per year injection, provide a useful alternative in ensuring patient compliance.

#### **About the Roche/GSK Alliance**

In December 2001, Roche and GlaxoSmithKline announced that they will co-develop and co-promote ibandronate for the treatment of postmenopausal osteoporosis. Roche and GSK plan to co-promote ibandronate in all countries, except Japan.

#### **About Roche**

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-oriented healthcare groups in the fields of pharmaceuticals, diagnostics and vitamins. Roche's products and services address prevention, diagnosis and treatment of diseases, thus enhancing well-being and quality of life. Roche sells its products in over 170 countries.

#### **Notes to editors**

With many current oral bisphosphonate therapies, patients on waking in the morning take the drug with a glass of water, then fast for up to an hour and are also supposed to remain standing during this time. This helps to prevent the drug binding to any calcium that is present in food – rendering it inactive - and to reduce the serious risk of oesophageal ulceration. Many patients find following this regimen very incompatible with their daily lives and routines and so discontinue therapy. Even more so for elderly patients who are frailer and are already taking multi-medication. In addition bisphosphonates commonly cause gastrointestinal (GI) disturbances - indigestion, diarrhoea and constipation-. These side effects combined with the strict administration routine often lead to poor patient compliance.

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# Media Release



Basel, 15 May, 2002

## Roche wins patent dispute with Chiron on Herceptin

The German District Court of Dusseldorf announced that Herceptin (Trastuzumab), one of Roche's leading oncology products, does not infringe a patent held by Chiron and therefore Roche is not required to pay royalties to Chiron.

Chiron filed its lawsuit against Roche in February 2001 and asserted that Roche infringed their patent directed to mouse monoclonal antibodies. According to the court's decision Chiron's patent does not embrace Herceptin.

Herceptin is a humanized monoclonal antibody directed to the HER2 protein and is a new, targeted approach developed for the treatment of metastatic breast cancer. Herceptin is the first oncogene targeted treatment with proven survival benefit in metastatic breast cancer, resulting in improved outcomes when used alone or in combination with chemotherapy. Herceptin is now approved in more than 40 countries throughout the world for the treatment of metastatic breast cancer.

### Roche in Oncology

Roche is a world leader in oncology. Its franchise includes three drugs with survival benefit: MabThera (non-Hodgkin's lymphoma), Xeloda (colorectal cancer, breast cancer), and Herceptin (breast cancer), it also includes NeoRecormon (anaemia in various cancer settings), Roferon-A (leukaemia, Kaposi's sarcoma, malignant melanoma, renal cell carcinoma), Neupogen (neutropenia) and Kytril (chemotherapy and radiotherapy-induced nausea). Roche Oncology has four research sites (two in the US, Germany and Japan) and four HQ Development sites (two in the US, UK and Switzerland).

### **About Roche**

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-oriented healthcare groups in the fields of pharmaceuticals, diagnostics and vitamins. Roche's innovative products and services address needs for the prevention, diagnosis and treatment of diseases, thus enhancing well-being and quality of life.

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# Media Release



Basel, 16 May, 2002

## **Positive Results from Second Phase III Study of HIV Fusion Inhibitor T-20 (enfuvirtide)**

**Second of two pivotal studies also meets primary endpoint; EU and US registration packages to be filed as planned**

Roche and Trimeris Inc today announce positive 24 week results from the second pivotal Phase III study of T-20 (TORO 2), just four weeks after reporting similarly positive 24-week results from the first Phase III study of T-20 (TORO 1). Together, these studies will form the basis of the submission to regulatory authorities. T-20 is the furthest in clinical development of a new class of investigational anti-HIV drugs known as "fusion inhibitors". Unlike existing AIDS drugs which work once the HIV virus has entered the host cell, T-20 has a novel mode of action in that it blocks HIV from entering and infecting human cells.

The results from the TORO 2 study show that T-20 administered in combination with an optimised antiretroviral treatment regimen provides a significant additional decrease in the amount of virus in the blood as compared to an optimised antiretroviral treatment regimen alone. TORO 2 was conducted in 504 HIV infected patients in Europe and Australia who were treatment-experienced and/or had documented resistance to each of the three classes of currently available anti-HIV drugs.

"This is the second large study demonstrating that T-20 provides a significant antiviral benefit for people living with drug resistant HIV" said William M. Burns, Head of Pharmaceuticals, Roche.

"The excellent results from the TORO 2 study confirm and build upon the results of the first pivotal Phase III study TORO 1. Taken together, these data represent a significant milestone in our commitment to deliver new treatment options for treatment experienced patients, particularly those living in the shadow of drug-resistant HIV".

At baseline, patients had a median HIV RNA level of over 5 log<sub>10</sub> copies/mL and extensive prior exposure to multiple anti-HIV drugs. At 24 weeks, patients who received T-20 as part of their combination regimen achieved a mean reduction in HIV levels of 1.43 log<sub>10</sub> copies/mL compared to a mean of 0.65 log<sub>10</sub> copies/mL for those who were randomised to the control arm, calculated in accordance with the study protocol. The primary efficacy endpoint for the study, the difference in the magnitude of decrease in HIV between the two arms at 24 weeks, was 0.78 log<sub>10</sub> copies/mL and was statistically significant (p < 0.0001). Roche and Trimeris expect to present these data in detail at scientific conferences in the next several months.

"The positive results from TORO 2 are both clinically and statistically significant. It is remarkable that both TORO studies consistently demonstrate the substantial treatment effect of T-20 across a diverse, treatment-experienced patient population from a number of countries. The Roche and Trimeris collaboration plan to proceed with filing registration packages for T-20 in the EU and US as planned early in the second half of this year," said Dr. Dani Bolognesi, Chief Executive Officer, Trimeris. "This important milestone brings T-20, the first member of a new class of antiretrovirals, yet another step closer to patients in need."

#### **Safety Results**

Through 24 weeks, as in TORO 1, overall clinical adverse events aside from injection site reactions were similar between T-20 and control groups. Other adverse events (>10%) occurring more frequently in the T-20 group were headache, fever, and asthenia. It was not possible to establish a causal relationship between these other adverse events and T-20. Grade 3 laboratory abnormalities were more frequent in the T-20 group, and Grade 4 laboratory abnormalities were more frequent in the control group. In TORO 2, discontinuation at 24 weeks was 17% in the T-20 group and 5% in the control group. Patients experiencing virological failure in the control group could switch to a T-20 regimen and not discontinue the study. While most patients on the T-20 arm experienced injection site reactions, only 3% of patients discontinued the study as a consequence.

#### **Early Access to T-20**

In November 2001, Roche and Trimeris announced the initiation of the T-20 open-label safety study (T20-305) to provide T-20 to 450 patients around the world. The study is ongoing and is being conducted in Australia, Brazil, Europe and North America. Roche and Trimeris are committed to starting early access programmes in the second half of this year when increased drug supply is expected to be available. Activities to build up the production capacity are on schedule.

## **Notes to editors**

### **Study Design**

TORO 2 (T-20 vs. Optimized Regimen Only), previously known as T20-302, and TORO 1 (previously known as T20-301) are randomized, open-label trials that enrolled approximately 1,000 patients at 112 centers worldwide. TORO 2 is being conducted in Australia, Belgium, France, Germany, Italy, The Netherlands, Spain, Sweden, Switzerland and the United Kingdom, TORO 1 is being conducted in North America and Brazil. Patients in the trials were treatment-experienced and/or had documented resistance to each of the three classes of currently-available antiretrovirals. In addition, each patient was required to have a plasma HIV-RNA level of greater than 5,000 copies/mL. Patients are expected to undergo treatment for 48 weeks, with an optional 48-week treatment extension. At entry, genotypic and phenotypic resistance testing was used to aid in the selection of an antiretroviral regimen, consisting of three to five drugs, including if appropriate, up to two newly approved or investigational drugs. After selection of the regimen, patients were randomized 2:1 to receive either the regimen in combination with T-20 or the regimen alone. Patients randomized to T-20 receive T-20 administered as one 90 mg subcutaneous self-injection twice-daily.

### **Meeting the Growing Need For a New Class of HIV Drugs**

One of the biggest challenges facing people living with HIV is resistance to currently available therapies. Thirty to fifty percent of patients are infected with a strain of the virus that has developed resistance to one or more antiretrovirals, thereby reducing the treatment options available to them. Roche and Trimeris are committed to discovering and developing treatments for patients in need of new options and expect to invest approximately half a billion U.S. dollars to bring fusion inhibitors to people living with HIV/AIDS.

### **Long-Term Commitment to HIV Research and Development**

Roche and Trimeris are working together to mobilize the considerable resources required to support the rapid development of T-20, the first member of a new class of investigational anti-HIV drugs known as fusion inhibitors. T-20, currently in Phase III clinical trials, is the furthest along in clinical development in the entry inhibitor class. T-1249, a second generation fusion inhibitor being developed by Roche and Trimeris, is in Phase I/II clinical trials. Unlike existing AIDS drugs that work inside the cell and target viral enzymes involved in the replication of the virus, T-20 inhibits fusion of HIV with host cells before the virus enters the cell and begins its replication process. In June 2001, Roche and Trimeris announced a joint research agreement to identify and develop additional HIV fusion inhibitor peptides.

T-20 has fast track designation from the FDA in the U.S. for the treatment of HIV-infected individuals. Fast track is granted to facilitate the development and expedite the review of applications for drugs that are intended to treat serious or life-threatening disease and that demonstrate the potential to address an unmet medical need.

#### **About Trimeris, Inc.**

Trimeris is a development stage, biopharmaceutical company engaged in the discovery and development of novel therapeutic agents that block viral infection by inhibiting viral fusion with host cells. Trimeris' lead product candidate, T-20, which inhibits fusion of the human immunodeficiency virus (HIV) with host cells, is currently in Phase III clinical trials and has received fast track designation from the FDA. Trimeris' second fusion inhibitor product candidate, T-1249, which also inhibits HIV fusion, has received fast track designation from the FDA and is in Phase I/II clinical testing. For more information on Trimeris, Inc., visit the company's Web site at [www.trimeris.com](http://www.trimeris.com)

#### **Trimeris Safe Harbor Statement**

Note: Except for any historical information presented herein, matters presented in this release are forward-looking statements that involve risks and uncertainties. The results of Trimeris' previous clinical trials are not necessarily indicative of future clinical trials, and future results could differ materially from the results presented herein. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the "Risk Factors" section included in Trimeris' Form 10-K for the year ended December 31, 2001 filed with the Securities and Exchange Commission on March 25, 2002.

#### **About Roche**

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-oriented healthcare groups in the fields of pharmaceuticals, diagnostics and vitamins. Roche's innovative products and services address needs for the prevention, diagnosis and treatment of disease, thus enhancing people's well-being and quality of life. For more information on Roche and its commitment to research in HIV, visit the: [roche-hiv.com](http://roche-hiv.com) website.

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