



Investor Update

Friday, October 29, 2004 8:01 AM

**European Commission approves further diagnostic testing methods for determining eligibility of patients for Herceptin  
Usage of wider range of HER2\* tests allows for optimal test results**

Roche announced today that the European Commission has approved the use of additional diagnostic testing methods for determining HER2 status of metastatic breast cancer patients to select who may benefit from Herceptin (trastuzumab) treatment. HER2-positive breast cancer patients suffer from a particularly aggressive form of breast cancer with a poor prognosis. Herceptin is the only targeted treatment for HER2-positive breast cancer with demonstrated improved survival, so early and accurate determination of HER2 status is imperative.

"The approved use of a wider range of diagnostic tests will provide more options and flexibility for determining the HER2 status of breast cancer tumours and an opportunity to obtain a second opinion when initial testing proves inconclusive," said Stefan Manth, Head of Roche Oncology. "This will ultimately help to improve breast cancer tumours' being correctly classified, and therefore patients' being treated appropriately."

Herceptin was previously approved in Europe for use in metastatic breast cancer patients whose tumours were tested as HER2-positive (so called "HER2 overexpression") only by the immunohistochemistry (IHC) testing method. However, in recent years, new "gene amplification" methods, namely fluorescence in situ hybridisation (FISH) and chromogenic in situ hybridisation (CISH), have also proven reliable in determining HER2 status. Use of these new methods in addition to the IHC method has become routine clinical practice in several European countries, and is already recommended in a number of European and international HER2 testing guidelines. This approval reflects the recent progress in HER2 testing and widespread usage of these alternative diagnostic methods: eligibility for Herceptin treatment can now be determined by tumours' having either HER2 overexpression or HER2 gene amplification, as determined by an accurate and validated assay.

**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\*\*. 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.

In HER2-positive breast cancer, increased quantities of the HER2 protein are present on the surface of the tumour cells. This is known as 'HER2 positivity.' High levels of HER2 are present in a particularly aggressive form of the disease which responds poorly to chemotherapy. Research shows that HER2-positivity affects approximately 20-30% of women with breast cancer\*\*\*.

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 where anthracyclines are unsuitable, 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.

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#### About 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, MabThera and Avastin are marketed either by Genentech alone or 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, 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 the 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.

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 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 number one in the global diagnostics market, 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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Please visit [www.HER2status.com](http://www.HER2status.com) and [www.heratrial.com](http://www.heratrial.com) for further information about Herceptin.

\* Human Epidermal growth factor Receptor 2

\*\* World Health Organization, 2000

\*\*\* Roche data on file

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## Investor Update

Wednesday, October 27, 2004 10:23 AM

### **Record number of Pegasys and Copegus abstracts accepted at the American Association for the Study of Liver Diseases (AASLD) conference Six oral presentations and 38 posters on Hepatitis C and B including two head-to-head studies**

A record 38 posters and six oral presentations will feature data about Pegasys and Copegus the 55th Annual Meeting of the American Association for the Study of Liver Diseases in Boston (October 29 - November 2). Pegasys and Copegus is the market leader worldwide in the treatment of chronic hepatitis C and the only pegylated interferon to be submitted to regulatory authorities worldwide for approval for the treatment of chronic hepatitis B.

Among the most significant abstracts and presentations are data from two head-to-head studies: one each in hepatitis C and B. Comparative data is valued by physicians as it offers them the opportunity to evaluate two drugs within the same trial rather than trying to analyze data across trials where variables such as patient demographics, drug dosages or study design can make comparisons meaningless.

The studies include:

- A U.S. head-to-head trial comparing Pegasys with PEG-Intron (peginterferon alfa-2b) in patients infected with difficult-to-treat genotype 1 hepatitis C virus that examines pharmacokinetics and pharmacodynamics - the action of the drug in clearing virus.
- The largest registration trial ever conducted in patients with HBeAg-positive chronic hepatitis B - the most common form of this disease - comparing Pegasys with lamivudine. This data will be presented for the first time.

In addition, two studies focus on hepatitis C patients who failed to respond to previous therapies, including peginterferon alfa-2b and ribavirin. Non-responders are among the fastest growing and most difficult-to-treat group of patients. New data from the U.S. and Spain will be presented demonstrating improved outcomes for re-treating these patients with Pegasys and Copegus.

Information contained within abstracts accepted for AASLD is under embargo from release by the press to the general public until October 29, 2004. The text of abstracts selected for presentation as well as the meeting schedule can be accessed on-line at <http://www.aasld.org>. Click on "Annual Meeting", then "Abstracts-Activity Planner" and "Online Abstract Viewer and Itinerary Planner". A detailed overview of submitted Pegasys abstracts can also be found on our website: <http://www.roche.com/home/investors.htm>

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## Media Release



Basel, 27 October 2004

### **Roche and Pharmasset join forces to develop new generation hepatitis C therapies**

Roche and Pharmasset today announced a partnership to develop nucleoside polymerase inhibitors for the treatment of chronic hepatitis C virus (HCV) infections. Pharmasset will receive an upfront fee, research and development support, and milestone payments that could total \$168 million for PSI-6130, the lead nucleoside compound of the partnership. In addition, Pharmasset will receive royalties on product sales and retain certain co-promotion rights in the US.

PSI-6130 has the potential to offer greater efficacy and activity against the hepatitis C virus, especially when used in combination with Roche's Pegasys and Copegus. For patients not responding to today's standard of care therapy, the addition of nucleoside polymerase inhibitors to their treatment regimen may offer benefit.

"Pharmasset's expertise in nucleoside drug discovery and early stage clinical development combined with Roche's proven track record in bringing new and improved hepatitis C therapies to market is a formula for success," stated Schaefer Price, Pharmasset's President and CEO. "The economics of this deal are significant. In addition, this partnership will support Pharmasset's activities toward establishing a commercial infrastructure for our HIV and HCV clinical candidates."

"We believe that nucleosides are likely to be an important new class of drugs in HCV treatment," said Jonathan K.C. Knowles, President of Global Research Roche. "PSI-6130 fits perfectly within our virology portfolio. When used in combination with Pegasys and Copegus, this therapy may offer significant benefit to patients who have previously been

resistant to treatment, especially those with a difficult to treat virus.”

Under the terms of the agreement, Roche will gain worldwide rights, excluding Latin America and Korea, to Pharmasset's PSI-6130 and its prodrugs. Pharmasset will be responsible for preclinical work, investigational new drug (IND) filings, and phase I proof of concept studies, with Roche managing other preclinical studies and clinical development. Roche will also receive options to related nucleoside polymerase inhibitors, which, if exercised, could result in Pharmasset receiving in excess of \$300 million in total milestones under the agreement. Pharmasset will continue to develop and retain worldwide rights to ongoing and future hepatitis C programs unrelated to the PSI-6130 series of nucleoside polymerase inhibitors. In addition, the Roche Venture Fund has made a \$4 million investment in Pharmasset and has received warrants to purchase an additional \$6 million in shares within the next two years, at a premium price.

#### **About HCV**

Hepatitis C is a blood-borne infectious disease of the liver and the leading cause of cirrhosis and liver cancer and the number one reason for liver transplants in the U.S. An estimated 2.7 million Americans are chronically infected with hepatitis C.

#### **About Pharmasset**

For more information about Pharmasset, please visit [www.pharmasset.com](http://www.pharmasset.com).

#### **About Roche as a partner**

Roche is a valued partner to over 50 companies worldwide. In 2003, Roche led the pharmaceutical industry in the number of product deals signed, bringing 10 potential products into the company, including a new antibiotic, a novel treatment for rheumatoid arthritis, and a cardiovascular compound for diabetes. Roche's alliance strategy is to enable our partners to grow through a flexible and collaborative approach.

For more information about Roche, please visit [www.roche.com](http://www.roche.com).