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## Investor Update

Thursday, June 30, 2005 7:35 AM

### Second New England Journal of Medicine paper establishes Pegasys as a first-line therapy in chronic hepatitis B Pegasys offers greater benefit versus current standard of care

Results published today in the prestigious New England Journal of Medicine (NEJM) have led the study authors to recommend Pegasys as a first-line treatment for chronic hepatitis B. The results show that patients with the most common form of chronic hepatitis B are more likely to achieve lasting remission if they are treated with Pegasys (peginterferon alfa-2a (40KD)) compared with lamivudine, a current standard of care. (1)

These results and conclusions confirm those from another phase III study of Pegasys in chronic hepatitis B also published in the NEJM in 2004. That study showed Pegasys was more effective in achieving lasting remission than lamivudine in patients with a more difficult-to-treat form of the disease. (2) These authors also concluded that Pegasys can be considered as a first-line therapy for chronic hepatitis B.

"The study published this week shows that more patients treated with Pegasys achieved the important treatment goal called HBeAg seroconversion, compared with those treated with lamivudine," said Dr. George Lau, gastroenterologist at the Queen Mary Hospital, Hong Kong and lead author of the NEJM paper. "Patients whose hepatitis B is in remission after treatment with Pegasys are unlikely to need further treatment, and their risk of developing cirrhosis, liver failure and liver cancer is reduced. These are compelling reasons for using Pegasys as a first choice in hepatitis B."

#### Key results from the study

The trial presented in this week's NEJM enrolled a total of 814 patients with HBeAg-positive chronic hepatitis B from 15 countries. In this trial, patients were treated for 48 weeks with Pegasys 180 mcg once weekly plus placebo, lamivudine 100 mg once daily, or a combination of Pegasys and lamivudine. Treatment response was assessed following a 24-week treatment-free follow-up period.

#### Six months after the completion of therapy:

- 32% of patients treated with Pegasys achieved HBeAg seroconversion\*, compared with 19% of those treated with lamivudine. The addition of lamivudine to Pegasys did not improve the treatment outcome (27% achieved HBeAg seroconversion).
- Importantly, HBsAg seroconversion was reported in 16 patients treated with Pegasys (with or without lamivudine) and in none of the patients treated with lamivudine alone. HBsAg seroconversion drastically reduces the risk of developing liver cancer or cirrhosis and is rarely seen during clinical trials. This event is considered as close to a cure for hepatitis B as is possible.

The two NEJM trials are part of one of the largest clinical development programmes in chronic hepatitis B which includes three global studies in more than 1,500 patients from 19 countries. The results of these trials demonstrate that Pegasys was more effective than lamivudine and conventional interferon in achieving lasting remission.(1,2,3)

"Chronic hepatitis B is a devastating disease that affects a huge number of people around the world," said Charles Gore, President of the European Liver Patients Association. "We welcome the efforts being made by pharmaceutical companies to develop increasingly effective drugs to combat it. The approval of Pegasys is a step forward in treatment options for patients with hepatitis B."

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Pegasys is currently undergoing regulatory approval around the world and has received approval for the treatment of chronic hepatitis B in over 40 countries including recent approvals in China and the United States, as well as in the EU. Pegasys is the first and only pegylated interferon to be indicated for the treatment of chronic hepatitis B.

Pegasys works to fight the disease in two ways: it boosts the immune system and at the same time, attacks the virus directly. Lamivudine, like other medications in its class, has a direct antiviral effect only and tends to be taken indefinitely as the hepatitis B often comes back if patients stop taking it. However, the virus can become resistant to lamivudine with long-term use, limiting the effectiveness of the medication.

This latest publication takes the total number of Pegasys publications in the NEJM to seven, the highest number of NEJM publications for any pegylated interferon.

#### About Chronic Hepatitis B

Chronic hepatitis B is a serious global healthcare problem that affects over 350 million people worldwide. It is one of the principal causes of chronic liver disease, cirrhosis, and primary liver cancer. Approximately one million die from chronic hepatitis B annually, making it the 10th leading cause of death worldwide. For those chronically infected, the immediate aim of treatment is remission of liver disease to prevent progression to cirrhosis, liver failure and primary liver cancer.

#### About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. As a supplier of innovative products and services for the early detection, 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 a world leader in diagnostics, the leading supplier of medicines for cancer and transplantation and a market leader in virology. In 2004 sales by the Pharmaceuticals Division totalled 21.7 billion Swiss francs, while the Diagnostics Division posted sales of 7.8 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. Additional information about the Roche Group is available on the Internet ([www.roche.com](http://www.roche.com)).

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\* HBeAg seroconversion is recognised by the AASLD as the recommended endpoint of treatment

#### Notes for the editor (recent Pegasys announcements):

US approval for the treatment of patients with chronic hepatitis B on May 16, 2005.

EU approval for the treatment of patients with chronic hepatitis B on February 25, 2005.

Swiss approval for the treatment of patients with chronic hepatitis B on December 22, 2004.

US approval for Pegasys in HCV/HIV co-infected patients on February 25, 2005.

EU approval for Pegasys in HCV/HIV co-infected patients on January 26, 2005.

EU approval for HCV patients with 'normal' ALT on November 11, 2004.

#### References:

- 1 Lau GKK, Piratvisuth T, Luo KX, et al. N Engl J Med 2005;2682-2695.
- 2 Marcellin P, Lau GK, Bonino F, et al. N Engl J Med 2004;351:1206-17.
- 3 Cooksley WG, Piratvisuth T, Lee SD, et al. J Viral Hepat 2003;10:298-305.

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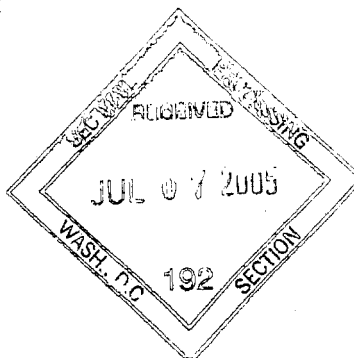
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# Media Release



Basel, 29 June 2005

## US Court of Appeals decides in favour of Roche on Empagran case

Roche announced today, that the District of Columbia Circuit Court of Appeals decided on June 28 that U.S. courts have no jurisdiction in the United States of America to claims of foreign purchasers of vitamins.

This decision brings to an end an initiative (so called "Empagran case") by non-US plaintiffs who wanted to bring claims in US courts under US anti-trust laws for alleged damages suffered from transactions outside the United States in connection with the vitamin case.

Gottlieb Keller, Head of Corporate Services and member of the Corporate Executive Committee stated: "We are satisfied by the decision of the Court of Appeals. We always felt strongly in our position. After the positive decision of the Supreme Court in June 2004 on 5 of 6 points, the Court of Appeals now also took a decision in favour of Roche on the remaining point."

### Background

On 17 January 2003 the District of Columbia Circuit Court of Appeals ruled that non-US plaintiffs may bring claims in US courts under US anti-trust laws for alleged damages suffered from transactions outside the United States in connection with the vitamin case. The defendants, including Roche, had filed a petition asking the Supreme Court to review the case. Mid of June 2004 the Supreme Court of the United States decided unanimously that non-US plaintiffs in principle may not bring claims in US courts for alleged damages suffered from transactions outside the US. The Supreme Court stated further, that the lower court (Court of Appeals) had not addressed one argument ("alternative theory") and that therefore plaintiffs remained free to ask the lower court to consider this argument.

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