# *Media Release*

Roche





Basel, 18 September 2002

## Roche's ribavirin Copegus available in all EU Countries within months

### Hepatitis C drug completes Mutual Recognition Procedure in the European Union



Roche announced today that it had received confirmation that the Mutual Recognition Procedure has been completed for its proprietary ribavirin, Copegus. This important milestone means that all EU member states have agreed to approve Copegus for the treatment of chronic hepatitis C in combination with interferon alfa-2a (Roferon A) or peginterferon alfa-2a (40 KD) (Pegasys).

"Today's approval of our stand-alone application means that we have satisfied all European Union member states of the safety and efficacy of the Copegus/ Pegasys combination treatment in patients infected with the hepatitis C virus ," said William M. Burns, head of the pharmaceutical division at Roche, adding that "this paves the way for the commercial availability of Copegus in all EU countries within one to three months. This is very important news as combination therapies are now standard for the treatment of hepatitis C."

The Dutch Medicines Evaluation Board, as the EU Reference Member State, first approved Copegus on April 9th which started this two-step approval process. National approvals will follow swiftly as Copegus is now an approved drug. Copegus is manufactured by Roche as a light pink, oval shaped, film-coated tablet containing 200 mg of ribavirin.

Copegus is indicated for the treatment of adult patients with chronic hepatitis C who have not previously been treated, including patients with fibrosis or compensated cirrhosis. It is also indicated for the treatment of adult patients who have responded to interferon alpha monotherapy but have since relapsed. Copegus is always prescribed as a combination regimen with interferon alfa-2a (Roferon A) or peginterferon alfa-2a (40 KD) (Pegasys).

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**About Pegasys**

Pegasys, a new generation hepatitis C therapy that is different by design, provides significant benefit over conventional interferon therapy in patients infected with HCV of all genotypes. The benefits of Pegasys are derived from its new generation large 40 kilodalton branched-chain polyethylene glycol (PEG) construction, which allows for true seven-day viral suppression and is preferentially distributed to the liver, the primary site of infection. Pegasys is administered once weekly in an easy-to-use pre-filled syringe with a fixed 180 mcg starting dose for all patient types.

Pegasys has now been approved in 47 countries, including the European Union. In the EU, it is indicated for the treatment of histologically proven chronic hepatitis C in adult patients, including patients with early stage cirrhosis. It is approved both as a combination therapy with ribavirin and as monotherapy. In the United States, Pegasys in combination with Copegus was granted a priority review by the FDA and its approval is anticipated later this year.

**About Hepatitis C**

Hepatitis C is a serious blood-born viral infection that attacks the liver, and in many patients it leads to liver disease, cirrhosis and cancer. It is the leading cause of liver transplantation. Only identified in 1989, the HCV virus has infected more than 170 million people world-wide, making it more common than the HIV virus.

**About Roche**

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-orientated healthcare groups. The company's two core businesses in pharmaceuticals and diagnostics provide innovative products and services, that address prevention, diagnosis and treatment of diseases, thus enhancing people's health and quality of life. The two core businesses achieved a turnover of 13,1 billion Swiss Francs in the 1st half of 2002 and employed about 57'000 employees worldwide.

Roche is committed to the viral hepatitis disease area, having introduced Roferon-A for hepatitis C, followed by Pegasys in hepatitis C, with studies currently being conducted on its efficacy in hepatitis B. Roche also manufactures The COBAS AMPLICOR™ HCV Test, v2.0 and the AMPLICOR HCV MONITOR™ Test, v2.0 - two tests used to detect the presence of, and quantify, HCV RNA in a person's blood. Roche's commitment to hepatitis has been further reinforced by the in-licensing of Levovirin, an alternative antiviral. Levovirin will be studied with the objective of demonstrating superior tolerability over the current standard, ribavirin.

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## Regulatory filing for first HIV Fusion Inhibitor Fuzeon (T-20)

Roche and Trimeris announce the submission of a New Drug Application to the US FDA for Fuzeon (enfuvirtide, T-20) for HIV-1 infection in combination with other antiretroviral agents and the plan to submit the Marketing Authorisation Application to the EU by the end of September. Moreover, Roche and Trimeris also announce that the completion of the next manufacturing milestone at the Roche Colorado manufacturing facility – completion of three validation batches – has been successfully achieved.
The submissions are based on the outstanding phase III results, which generated considerable interest when presented at the International Aids Congress in Barcelona in July.
The data are better than expected and show that heavily treatment experienced patients are twice as likely to achieve undetectable HIV levels plus have an improved immunological status when Fuzeon is combined with other antiretroviral agents compared to taking antiretroviral agents without Fuzeon.

Fuzeon is the frontrunner in a new class of anti-HIV drugs called "fusion inhibitors". Unlike existing anti-HIV drugs that work inside the cell, Fuzeon has a unique mode of action and is designed to block HIV before entering the human immune cell. Fuzeon is active against HIV that is resistant to the currently available classes of anti-HIV drugs. As a result of the better than expected activity and tolerability data, Fuzeon offers new hope to patients with limited treatment options.

"The incidence of drug resistant HIV among already treated patients is increasing at a disturbing rate, with up to 78 percent of patients in North America and Europe infected with a strain of the virus that has developed resistance to one or more anti-HIV drugs", said Dr. Daniel Kuritzkes, Director of AIDS Research, Brigham and Women's Hospital, Associate Professor of Medicine,

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Harvard Medical School. "It is clear that the need for new drugs such as Fuzeon which work in completely new ways to block HIV will become ever more urgent."

William M. Burns, Head of Roche's Pharma Division, said "These filings are important steps for Roche. HIV is a constantly evolving virus, so it is no wonder that drug resistance has become one of the greatest HIV medical challenges physicians and patients are facing in the developed world today. Patients are now living with new and different types of HIV and need dramatically different therapies to help manage their disease. Fuzeon was one of the most difficult scientific and manufacturing challenges we have faced, but despite these challenges we have developed Fuzeon at the fastest pace possible in response to this increasing patient need. We proceeded in parallel across Europe and North America and now anticipate launches from the first quarter next year."

"Fuzeon was designed from the outset to block HIV replication in a completely different manner than current antiretroviral drugs, while not substantially adding to the toxicity of other agents. Fuzeon's unique mode of action is designed to block HIV before entering the human cell and if approved, it will represent the first of a new class of anti- HIV drug in seven years," said Dr. Dani Bolognesi, CEO, Trimeris. "These milestones are the latest result of the ongoing joint development programme between Roche and Trimeris."

Fuzeon is one of the most challenging molecules ever chemically manufactured at such a large scale by the pharmaceutical industry. One hundred and six manufacturing steps are required to produce the active drug substance alone, which is around ten times more than that of a protease inhibitor. To coincide with the fast paced clinical development program, the Roche Colorado manufacturing plant has been working 24 hours a day, seven days a week in the commercial scale-up of Fuzeon. Because of this dedication, the next major milestone for commercial manufacturing completion of three validation batches has been achieved and therefore, the process of bringing the commercial plant on hand for launch remains firmly on track. In addition, continued investments are being made in the ongoing development of the manufacturing facility to meet potential increased demand for Fuzeon.

Resistance to HIV drugs

It is estimated that in a single person the virus can mutate to form around a billion new and different versions of HIV in just 24 hours. The incidence of drug resistant HIV among already treated patients is increasing at a disturbing rate, with up to 78 percent of patients in North America and Europe infected with a strain of the virus that has developed resistance to one or more anti-HIV drug.

**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. Saquinavir was the first Protease Inhibitor (PI) and was first introduced by Roche in 1995 in the US.

As a consequence of Roche's continuous research and development, the combination of boosted saquinavir with ritonavir (1000/100 mg twice daily) has shown encouraging results in the MaxCmin 1 trial with high efficacy and an excellent safety and tolerability profile. Saquinavir/r was approved in the EU in August 2002. Viracept (nelfinavir), another PI is supplied by Roche outside the US and Canada. In first-line HIV therapy, Viracept delivers consistent long-term efficacy and safety. When used first line, Viracept also allows the subsequent use of both NNRTIs and other PIs for most patients due to its unique resistance pattern.

The viral load measurements in the clinical trials for Fuzeon were performed using the AMPLICOR HIV-1 MONITOR version 1.5 assay. 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 therapies- including a paediatric formulation- for these regions and research in HIV, visit the www.roche-hiv.com website.

**About Roche**

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**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, Fuzeon, 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

**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 S-3 filed with the Securities and Exchange Commission on August 23, 2002.