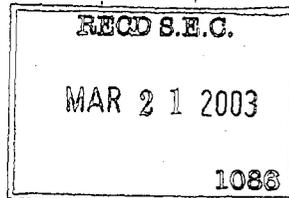


## Media Release



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Basel, 14 March, 2003



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### U.S. FDA Approves Fuzeon; First Drug to Block Entry of HIV into Immune Cells

**Fuzeon leads first new class of anti-HIV drugs since 1996**

Roche and Trimeris, Inc. (Nasdaq: TRMS) announced today that Fuzeon (enfuvirtide), a novel treatment for HIV-1, has been granted accelerated approval by the U.S. Food and Drug Administration (FDA) following a six-month priority review. Fuzeon in combination with other antiretroviral agents is indicated for the treatment of HIV-1 infection in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy.

Fuzeon is the first fusion inhibitor, representing the first new class of anti-HIV treatments in seven years. Unlike all currently approved anti-HIV drugs, Fuzeon blocks the virus from entering the human immune cell, preventing HIV replication that can devastate the immune systems of HIV infected individuals.

"Fuzeon is yet another example of Roche's long-standing commitment to advancing the treatment of HIV," said William Burns, Head of Roche Pharma. "Fuzeon represents a major advance in the fight of HIV/AIDS. As more and more people with HIV are running out of options due to HIV drug resistance, new options are urgently required. With its novel mode of action Fuzeon meets this growing need. Fuzeon also represents a major advancement in the large-scale chemical synthesis of peptides. This cutting edge process has been successfully implemented at the Roche manufacturing facility in Boulder, Colorado."

"With Fuzeon, what we've essentially done is to take a piece of the virus and turn it against itself. The safety and efficacy of this new molecule were demonstrated through two rigorously-designed pivotal studies conducted in a diverse treatment-experienced patient population," said Dr. Dani Bolognesi, Chief Executive Officer, Trimeris. "Together with our partner Roche, Trimeris is proud to bring this innovative new therapy to the growing number of people with HIV who are in need of new treatment options."

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#### **Pivotal Data**

The regulatory submission for Fuzeon was based on data from two 24-week Phase III pivotal studies of approximately 1,000 patients, TORO (T-20/Fuzeon vs. Optimized Regimen Only) 1, conducted in North America and Brazil, and TORO 2, conducted in Europe and Australia. These studies showed that treatment-experienced patients receiving Fuzeon as a part of an optimized background regimen (individualized combination of anti-HIV drugs) experienced greater immunologic improvements and were twice as likely to achieve undetectable plasma levels of HIV (HIV-1 RNA of HIV<400 copies/ml.) compared to patients receiving an individualized regimen alone. In addition, those patients with two or more active drugs in their background regimen were more likely to achieve undetectable levels of HIV.

Because of the public health implications, The New England Journal of Medicine (NEJM) will post the clinical results from the Fuzeon TORO 1 study on its web site, [www.nejm.org](http://www.nejm.org) in advance of publishing the data in an upcoming issue.

#### **Supply and Distribution of Fuzeon**

Roche and Trimeris have committed to make Fuzeon available for distribution in the US before the end of March. Because initial demand for Fuzeon may exceed supply following commercial availability, Roche and Trimeris have developed and are now finalizing a US Progressive Distribution Plan to provide Fuzeon to patients and to ensure uninterrupted supply to patients once they begin therapy. The details of this US Progressive Distribution Plan will be announced in the near future.

#### **Approved Indication**

Fuzeon in combination with other antiretroviral agents is indicated for the treatment of HIV-1 infection in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy.

This indication is based on analyses of plasma HIV-1 RNA levels and CD4 cell counts in controlled studies of Fuzeon of 24 weeks duration. Subjects enrolled were treatment-experienced adults; many had advanced disease. There are no studies of Fuzeon in antiretroviral naive patients. There are no results from controlled trials evaluating the effect of Fuzeon on clinical progression of HIV-1.

#### **More About Fuzeon**

Fuzeon is administered as a twice-daily subcutaneous injection. Local injection site reactions were the most frequent adverse events associated with the use of Fuzeon. In Phase III clinical studies, 98 percent of patients had at least one local injection site reaction. The addition of Fuzeon to

background antiretroviral therapy generally did not increase the frequency or the severity of the majority of adverse events.

There was less than five percent difference in the most common adverse events seen between Fuzeon plus an individualized regimen of antiretroviral drugs and individualized regimen alone. The events most frequently reported in subjects receiving Fuzeon plus an individualized regimen were diarrhea (26.8%), nausea (20.1%), and fatigue (16.1%).

Hypersensitivity reactions have been associated with Fuzeon therapy (< 1 percent) and have recurred on rechallenge. In addition, an increased rate of bacterial pneumonia was observed in patients treated with Fuzeon in the Phase III clinical trials compared to the control arm. It is unclear if the increased incidence of pneumonia is related to Fuzeon use.

#### **Roche in HIV**

Roche is at the forefront of efforts to combat HIV infection and AIDS, committed for 15 years to groundbreaking research and development of new drugs and diagnostic technology. Roche's objective is to provide tailored treatment solutions and an improved standard of care worldwide for people living with HIV.

#### **About Roche**

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-oriented healthcare groups. The company's two core businesses, pharmaceuticals and diagnostics, develop and market innovative products and services aimed at preventing, diagnosing and treating disease and thus enhancing people's health and quality of life. In 2002 Roche's core businesses recorded sales of 26.5 billion Swiss francs and employed some 61,900 people worldwide.

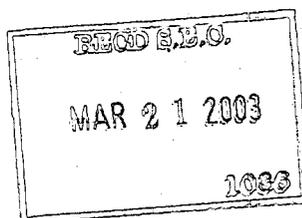
#### **About Trimeris, Inc.**

Trimeris, Inc. (Nasdaq: TRMS) is a biopharmaceutical company engaged in the discovery, development and commercialization of novel therapeutic agents for the treatment of viral disease. The core technology platform of fusion inhibition is based on blocking viral entry into host cells. Fuzeon, just approved by the FDA, is the first in a new class of anti-HIV drugs called fusion inhibitors. A Marketing Authorisation Application (MAA) has also been submitted for Fuzeon in the European Union. Trimeris' second fusion inhibitor product candidate, T-1249, has received fast track status from the FDA and is in Phase I/II clinical testing. Trimeris is developing Fuzeon and T-1249 in collaboration with F. Hoffmann-La Roche Ltd. For more information about Trimeris, please visit the company's website at [www.trimeris.com](http://www.trimeris.com).

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**Trimcris Safe Harbor Statement**

This document and any attachments may contain forward-looking information about the Company's financial results and business prospects that involve substantial risks and uncertainties. These statements can be identified by the fact that they use words such as "expect," "project," "intend," "plan," "believe" and other words and terms of similar meaning. Among the factors that could cause actual results to differ materially are the following: there is uncertainty regarding the success of research and development activities, regulatory authorizations and product commercializations; the results of our previous clinical trials are not necessarily indicative of future clinical trials; and, our drug candidates are based upon novel technology, are difficult and expensive to manufacture and may cause unexpected side effects. For a detailed description of these factors, see Trimcris' Form S-3 filed with the Securities and Exchange Commission on September 27, 2002 and its periodic reports filed with the SEC.



## Investor Update

March 14, 2003

**Pegasys® a more tolerable treatment for hepatitis C patients, study reveals**  
Health-related quality of life must be considered when selecting a treatment against chronic hepatitis C to ensure adherence to therapy", authors say

Two weeks after initiating treatment with Pegasys, a new study has found that hepatitis C patients experienced significantly less fatigue, pain, physical and emotional limitations, and had improved vitality compared to patients treated with conventional interferon. Notably, maintaining health-related quality of life during treatment may reduce the risk of early treatment discontinuation. The study is published in the current issue of *Pharmacoeconomics*.

"We know that many patients do not adhere to their hepatitis C treatment because the side effects are often considered by patients to be more objectionable than the symptoms of the disease," said Dr. Jens Rasenack, the study author and Professor of Medicine in the department of Gastroenterology and Hepatology at the Albert-Ludwigs-University of Freiburg Germany. "The positive impact that Pegasys has on health-related quality of life makes it more likely that they will complete their treatment and ultimately improve their chances of being cured."

Previous studies have demonstrated that interferon therapy has a negative effect on health-related quality of life (HRQL) during the initial three to six months of therapy. Patients typically experience side effects such as flu-like symptoms, fatigue, lack of energy, body pain and alterations in mood, making it difficult for them to participate in every day activities.

Patients treated with Pegasys demonstrated significantly better scores in all health areas surveyed compared to those treated with conventional interferon and reported less disabling fatigue. The less disabling fatigue that Pegasys-treated patient experienced is thought by the study authors "to be attributed to the near-constant and sustained serum levels produced by the weekly dosing regimen of peginterferon alfa-2a (40KD) compared with the peaks and troughs associated with thrice weekly administration of unmodified interferon alfa-2a."

The patients treated with Pegasys also reported fewer problems with work due to physical or emotional problems and were less likely to report lacking pep or energy, being tired or feeling worn out. These patients were also less likely to report moderate or severe pain that interfered substantially with their work. These benefits continued for at least the first 12 weeks of treatment and in some cases right up to the 48th week of treatment.

The authors note that this analysis further extends the understanding of the documented benefits of Pegasys' better tolerability. Given that worsening health-related quality of life while on treatment negatively influences compliance, the study authors conclude that "the impact of quality of life should be considered when selecting a treatment against chronic hepatitis C to ensure adherence to treatment."

#### About the study

The health-related quality of life analysis was based on an international multicentre, open-label, randomized dose efficacy and safety study comparing Pegasys with unmodified interferon alfa-2a. Patients received either the standard dose of Pegasys (180mcg once weekly) for 48 weeks or conventional interferon (6MIU thrice weekly for 12 weeks followed by 3 MIU thrice weekly for a further 36 weeks). Patients were followed until 72 weeks after the start of treatment. The study was conducted in 36 centres in Australia, Canada, Germany, Mexico, New Zealand, Spain, Switzerland, Taiwan and the United Kingdom and included 531 patients. The results of the study "Peginterferon alfa-2a (40KD) (Pegasys) improves health-related quality of life outcomes compared with unmodified interferon alfa 2-a in patients with chronic hepatitis C" are published in this month's issue of *Pharmacoeconomics*\*.

#### How quality of life and fatigue were measured

Patients' quality of life and levels of fatigue were assessed at 2, 12, 24, 48 and 72 weeks after the start of treatment. Quality of life and fatigue were measured using the internationally recognised Short Form 36 health survey and the Fatigue Severity Scale.

#### About hepatitis C

Chronic hepatitis C is a serious viral infection of the liver and the leading cause of liver damage throughout the world. As many as 3% of the world's population are infected with the hepatitis C virus. Those who develop chronic hepatitis C risk cirrhosis, liver cancer, liver failure and liver transplantation.

#### 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 constant viral suppression. Pegasys also distributes more readily to the liver (the primary site of infection) than conventional interferon. Pegasys is the only pegylated interferon available as a ready-to-administer solution. Each weekly subcutaneous injection contains 180mcg of pegylated interferon alfa-2a which is the recommended dose for all patients, regardless of body weight.

#### 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 19.3 billion Swiss Francs in the first three quarters of 2002 and employed about 57,000 people worldwide.

Roche is committed to the viral hepatitis disease area, having first introduced Roferon-A for hepatitis B and then C, followed by Pegasys in hepatitis C. Pegasys is also in phase III clinical development for patients infected with the HBV virus. Roche has also launched its own brand of ribavirin, Copegus, to be used in conjunction with Roferon A or Pegasys. Roche manufactures and sells the Amplicor HCV Test (v2.0) and the Amplicor HCV Monitor Test (v2.0) - two tests used to detect the presence of HCV RNA in a person's blood. The company's commitment to hepatitis is 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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The journal Pharmacoeconomics is available online at [www.ingenta.com](http://www.ingenta.com). Please note that broadcast reporters can download images to accompany stories from [www.thenewsmarket.com](http://www.thenewsmarket.com). Please search under "Roche".

\*Pharmacoeconomics 2003; 21 (5):1; Adis International Limited

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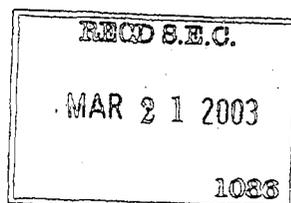
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## Media Release



Basel, 18 March 2003

### **Roche Diagnostics and Epigenomics sign broad Cancer Diagnostics alliance**

**Companies to collaborate on diagnostic products for early cancer detection, classification and treatment response**

Roche and Epigenomics announced today a broad three-year collaboration to develop a range of molecular diagnostic and pharmacogenomic cancer products based on Epigenomics' DNA-methylation technologies. DNA Methylation is a natural "switch" that controls gene expression giving rise to distinct patterns in cells including cancer and other diseased cells. Based on these methylation patterns, cancer can be detected and classified from tissue and bodily fluids, such as blood serum or urine samples.

Under the terms of the agreement, Roche will make an upfront payment of € 4 million and in addition provide R&D funding, milestone payments and royalties on product sales. Both partners estimate that if all products are successfully launched, the total value of the agreement could exceed € 100 million.

The collaboration comprises the development of diagnostics products for use in early detection of cancers from major sites (e.g. colon, breast, prostate), their characterization (e.g. aggressive versus non-aggressive tumors) and prediction of treatment response to particular anti-cancer drugs. Epigenomics will be responsible for marker discovery, identification and pre-validation. Epigenomics' DNA methylation technologies will be incorporated into Roche's existing and future PCR platforms (PCR: polymerase chain reaction) and into the recently licensed Microarray Technology. Diagnostic test development, clinical trials, product manufacturing, regulatory submissions and all sales and marketing worldwide are to be conducted by Roche.

"We are very enthusiastic about this collaboration. Roche is already the world leader in cancer therapies and with this alliance we will complement our position in the diagnostics field. The products that are being developed as part of this collaboration address the urgent need for earlier detection of cancer in bodily fluids by more accurate screening tests, as well as identifying those patients who need chemotherapy and most likely respond to particular cancer therapies," says Heino von Prondzynski, Head of Roche Diagnostics and member of Roche's Corporate Executive Committee. "As the worldwide leader in *in vitro* Diagnostics we are committed to identify diseases early in order to improve treatment and enhance patients' quality of life. The alliance with Epigenomics will help us to remain at the forefront of the molecular diagnostics market and support our activities to pursue a market that could be greater than 3 billion Swiss francs ten years from now for our divisional cancer care program."

Alexander Olek, CEO of Epigenomics, adds: "This collaboration validates Epigenomics' DNA methylation technology and product development approach. By underlining the synergy between our in-house units, Diagnostics and Pharma Technology businesses, it allows us to pursue our vision of personalizing medicine. With the emerging trend of the pharmaceutical industry moving towards administering therapy only with a specific diagnostic test, we feel that the partnership with Roche Diagnostics solidifies Epigenomics' position as a leader in this field."

#### **DNA Methylation and Diagnostic Applications**

DNA methylation is a natural phenomenon whereby a methyl chemical group is attached to the cytosine base of DNA. The pattern of DNA methylation is one of the primary biological mechanisms that controls gene expression or activity. As the methyl group is either present or not, the pattern on any strand of DNA can be digitized and easily interpreted. Measuring the differences in DNA methylation patterns of diseased and healthy conditions provides a reliable, sensitive and convenient way of identifying disease. For example, bodily fluid samples (e.g. blood serum or urine) can be used to reveal whether that person has cancer. Using a tissue sample from this individual, the DNA methylation patterns can be interpreted to show what type of cancer it is and most importantly guide physicians on the most appropriate way to treating it.

#### **Roche is the world leader in oncology treatment**

Roche Diagnostics offers a broad portfolio of tumor markers for prostate, colorectal, liver, ovarian, breast, stomach, pancreas and lung cancer, as well as a range of molecular oncology tests running on the LightCycler. Within its Integrated Cancer Care Unit the company develops new tests which will have a significant impact on disease management of cancer patients in the future. The franchise of its pharmaceuticals Division includes MabThera (non-Hodgkin's lymphoma),

Xeloda (colorectal cancer, breast cancer), Herceptin (breast cancer), NeoRecormon (anaemia in various cancer settings), Roferon-A (leukaemia, Kaposi's sarcoma, malignant melanoma, renal cell carcinoma) and Kytril (chemotherapy and radiotherapy-induced nausea). The franchise accounted in 2002 for sales of more than 5 billion Swiss francs (+33%).

#### About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-oriented healthcare groups in the fields of pharmaceuticals and diagnostics. Roche's products and services address prevention, diagnosis and treatment of diseases, thus enhancing well-being and quality of life. In 2002 Roche's core businesses recorded sales of 26.5 billion Swiss francs and employed some 61,900 people worldwide. Roche's Diagnostics Division, the world leader in *in vitro* diagnostics with a uniquely broad product portfolio, supplies a wide array of innovative testing products and services to researchers, physicians, patients, hospitals and laboratories world-wide. For further information, please visit the website at [www.roche.com](http://www.roche.com).

#### About Epigenomics

Epigenomics is committed to significantly improving the treatment of cancer and other complex diseases by developing novel diagnostic and pharmacogenomic products based on DNA methylation. By detecting and interpreting DNA methylation patterns, the "on" and "off" signs for genes, Epigenomics can create a digitized readout (Digital Phenotype®) for each cell. The comparison of a patient's cells against healthy and abnormal reference samples enables an exact diagnosis of disease at a very early stage and provides physicians with essential information to help guide an appropriate therapy. The combination of diagnosis and therapy, based on this information and robust proprietary technology, is "personalizing" medicine. Epigenomics is supported by a network of renowned academic researchers and clinicians, with expertise in the fields of cancer and DNA methylation. The company has its headquarters in Berlin, Germany, and a wholly owned subsidiary in Seattle, USA. For further information, please visit the website at [www.epigenomics.com](http://www.epigenomics.com).