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Subject: FW: Investor Update: Eur[redacted]ves New Boosted Saquinavir Regimen

—Original Message—
From: Ir-Internet, Basel (~Basel)
Sent: Thursday, September 19, 2002 10:41 AM
To: Kraehenmann, Beat (CLL~Basel)
Subject: Investor Update: European Commission Approves New Boosted Saquinavir Regimen

European Commission Approves New Boosted Saquinavir Regimen
(1000 mg Saquinavir / 100 mg Ritonavir twice daily)
With Impressive Potency for the Treatment of HIV-1
New regimen provides striking "boosted protease inhibitor potency" whilst maintaining an impressive safety and tolerability profile and lowering pill burden

Roche today announced that the Committee for Proprietary Medicinal Products (CPMP) has granted approval for both INVIRASE™ (saquinavir hard gel capsules) and FORTOVASE™(saquinavir soft gel capsules), to be co-administered with a low dose of ritonavir (1000 mg saquinavir/100mg ritonavir twice daily). *

Boosting saquinavir with low doses of ritonavir allows more saquinavir to be absorbed into the blood and keeps saquinavir in the body for longer. The benefit for patients is that by using this approach, highly potent therapeutic levels of saquinavir are achieved in the blood with an excellent safety and tolerability while it is possible to reduce the dosing frequency and the required number of capsules.

Dr. Calvin Cohen, Research Director - Community Research Initiative of New England and Harvard Vanguard Medical Associates commented: "Saquinavir is among our most potent HIV protease inhibitors. This new boosted regimen dramatically increases blood levels of saquinavir and this in turn translates into very potent HIV suppression - as illustrated by the MaxCmin 1 study. The two things that really struck me in this study was the magnitude of benefit that boosted saquinavir showed in the pre-treated patient group, together with the very good tolerability profile of the regimen".

"Saquinavir/ritonavir 1000/100 mg twice daily is an excellent option for patients who require a boosted protease inhibitor, including those who have experienced toxicity or virological failure with a prior protease inhibitor-containing regimen." Said Dr. Mike Youle, Director, HIV Clinical Research at the Royal Free Centre for HIV Medicine, London.

The European Commission's approval of this new regimen was based partly upon preliminary data from an independent collaborative investigator group, the Copenhagen HIV Programme (CHIP). The MaxCmin 1 study evaluated 317 patients in 14 countries across Europe, South America and the US and compared the new boosted saquinavir regimen with ritonavir-boosted indinavir. The final 48-week results of the MaxCmin 1 study showed that the "boosted" saquinavir regimen reduced the levels of HIV in patients' blood to below detection (<400 copies/mL) in a significantly greater proportion of patients (68%) than those who were administered boosted indinavir (53%).

For patients who remained on their study medication, HIV-1 virus was suppressed to an undetectable level in 93% and 90% of patients on the boosted saquinavir and indinavir regimens, respectively. However, significantly more patients withdrew from the study due to side effects in the boosted indinavir patient group (41%) versus the boosted saquinavir patient group (28%). Furthermore, cholesterol and triglyceride levels increased more in the boosted indinavir patient group versus the boosted saquinavir group**. There are growing concerns regarding the potential impact of such increases in triglyceride and cholesterol levels on the chance of patients developing cardiovascular events and lypodystrophy.

More about saquinavir
Saquinavir is a member of the class of anti-HIV drugs known as protease inhibitors (PIs). PIs block a part of the HIV reproduction process involving the HIV protease, thus preventing the formation of new infectious HIV particles. Saquinavir is almost always used in combination with at least two other anti-HIV drugs and has been shown to significantly improve survival and reduce the occurrence of AIDS-defining events for people infected with HIV. Saquinavir is not a cure for HIV.

dlw 9/23

The new saquinavir/ritonavir regimen is also recommended in the new draft of the WHO guidelines "Scaling up antiretroviral therapy in resource limited settings: Guidelines for a public health approach" (reference will be inserted).

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 innovative products and services address needs for the

prevention, diagnosis and treatment of disease, thus enhancing people's well being and quality of life.

Editors' Note:
*Boosted Saquinavir Regimen (1000 mg Saquinavir / 100 mg Ritonavir twice daily) was submitted for centralised approval, which means an authorisation is valid for the whole European Union. In this case the application was dealt with administratively by The European Agency for Evaluation of Medicinal Products (EMEA). A reporting country (Austria) and a co-reporting country (Sweden) were selected, and conducted independent evaluations. The reports were then sent to other member states and a decision was made by the European Commission after the scientific committee (Committee for Proprietary Medicinal Products, CPMP) of the EU has expressed an opinion.

The Commission Decision is valid for all EU countries, including Norway and Iceland. For all EU enlargement countries (CADREAC), an application has been submitted and is awaiting approval.

** Cholesterol and triglyceride levels in the boosted indinavir patient group versus the boosted saquinavir group: fasting total cholesterol 17% vs 9%, Low Density Lipid (LDL) cholesterol 21% vs 6% and triglyceride levels 29% vs 13% respectively.