March 1, 2005

Public Relations
Ono Pharmaceutical Co., Ltd.
TEL：+81-6-6263-5670
FAX：+81-6-6263-2950

New Data on New HIV Drug (Oral CCR5 Receptor Antagonist)

Ono Pharmaceutical Co., Ltd. (Ono) announced today that GlaxoSmithKline (GSK) presented new data on clinical pharmacology studies with 873140(ONO-4128) at the 12th Conference on Retroviruses and Opportunistic Infections held in Boston from February 22 to 25. 873140 (ONO-4128), an investigational HIV compound, was licensed to GSK by Ono in 2002 for worldwide development, manufacture and sales.

＜Sustained CCR5 inhibitory effect＞

873140 (ONO-4128) demonstrated prolonged CCR5 receptor occupancy. This suggests a potential mechanism for the sustained antiretroviral effect seen following 873140 (ONO-4128) administration in HIV-infected patients.

873140 (ONO-4128) demonstrated prolonged CCR5 receptor occupancy in both HIV-positive and HIV-negative individuals following repeat-dose administration. At sample times following the final dose, when plasma drug levels were undetectable, significant CCR5 receptor occupancy (>50%) was observed for approximately five days.

It has been confirmed that 873140 (ONO-4128) has showed sustained viral suppression for 24 to 48 hours after repeat-dose administration of therapy was discontinued in HIV-infected patients. The prolonged CCR5 receptor occupancy suggests a potential mechanism for the sustained antiretroviral effect of 873140 (ONO-4128).

<Pharmacokinetic Interactions Between 873140 (ONO-4128) and Kaletra®>

873140 (ONO-4128) was co-administered with Kaletra®(lopinavir/ritonavir), a common component of HIV therapy. The result showed that 873140 (ONO-4128) was well-tolerated as well as the concentration of 873140 (ONO-4128) in the plasma was significantly increased when co-administered with Kaletra®.

873140 (ONO-4128) was co-administered with Kaletra®(combination product of lopinavir and ritonavir) to explore the potential drug–drug interactions, as well as safety and tolerability in healthy

adult subjects.

The concentration of 873140 (ONO-4128) when given together in repeat dosing was significantly higher, indicating that the dose of 873140 (ONO-4128) can be reduced when co-administered with Kaletra®. In this study, the most common adverse events were Grade 1 gastrointestinal complaints that resolved within one to three days on therapy. There were no drug-related discontinuations from the study. The combination of 873140 (ONO-4128) and Kaletra® was well-tolerated and demonstrated an acceptable safety profile.

These results support the further evaluation of 873140(ONO-4128) with ritonavir-boosted protease inhibitor regimens in the future clinical studies.

The human CCR5 receptor is believed to be the predominant co-receptor used by HIV. 873140 (ONO-4128) appears to block the entry of HIV into human cells through a new mechanism of action that is totally different from those of currently available drugs. The likelihood of viral resistance caused by viral mutation may be lower for CCR5 antagonists since these CCR5 receptors exist on the surface of the human immune cell. Clinical resistance to CCR5 antagonists remains to be determined. The new data presented represent another step forward in the development of 873140, which may offer a novel treatment option for people living with HIV.

Based on data of safety, pharmacokinetics, drug-drug interactions, antiretroviral effect, CCR5 receptor occupancy from the Phase I study and the early Phase II clinical study, GSK has already commenced the late Phase II clinical studies at the end of 2004.

According to GSK, regulatory filings are expected in 2007 if the development goes well.
873140 was granted Fast Track designation by the US Food and Drug Administration in October 2004.

Note：Kaletra® is a combination product of lopinavir and ritonavir. Ritonavir is used to inhibit the major metabolic enzymes of lopinavir, resulting in boosting levels of lopinavir in the blood. Among anti-HIV drugs, some protease inhibitors aim to boost the blood concentration by inhibiting the major metabolic enzymes through co-administration with ritonavir in the same manner as Kaletra®.