



June 13, 2005

Ono Pharmaceutical Co., Ltd., Public Relations

Tel: +81-6-6263-5670

Banyu Pharmaceutical Co., Ltd., Public Relations

Tel: +81-3-5203-8105

Results of Phase II Studies of Sitagliptin (MK-0431 / ONO-5345) Investigational Treatment for Type 2 Diabetes Presented by Merck & Co., Inc. at ADA

In November 2004, Ono Pharmaceutical Co., Ltd. (Headquarters: Osaka, Japan) and Merck & Co., Inc. (Headquarters: Whitehouse Station, New Jersey, USA) signed licensing agreements under which Ono granted Merck worldwide development and marketing rights (except Japan, Korea, Taiwan) for ONO-2506 for injection, a novel compound developed by Ono for the treatment of acute stroke.

In connection with this license, Merck granted Ono rights to co-develop and co-market a second brand of sitagliptin (MK-0431 / ONO-5345), an investigational oral anti-diabetic agent, in Japan. Banyu Pharmaceutical Co., Ltd., Merck's subsidiary in Japan, will co-develop and co-market a separate brand of sitagliptin in Japan. In addition, Ono received exclusive rights in Japan to develop and market aprepitant (MK-0869 / ONO-7436), an investigational agent for the prevention of chemotherapy-induced nausea and vomiting.

Sitagliptin, which is in Phase II in Japan, is being developed by Banyu. Ono will participate with Banyu in Phase III development of sitagliptin in Japan. Aprepitant is currently in Phase II development in Japan by Ono.

The data from Phase II studies of sitagliptin were presented recently at the 65th Annual Meeting of the American Diabetes Association in San Diego, California, and Merck issued a press release as follows:

Sitagliptin (MK-0431), Merck's Investigational Treatment for Type 2 Diabetes, is Shown to be Efficacious and Well Tolerated in Phase II Clinical Trials

Results from three Phase II studies announced today support efficacy profile of new diabetes treatment

SAN DIEGO, June 11, 2005 – Results from three Phase II studies announced today, show that sitagliptin phosphate (MK-0431) was efficacious and well tolerated in patients with type 2 diabetes. In these studies of more than 1,000 patients, sitagliptin, Merck & Co., Inc.'s investigational medicine from a new class of agents for the treatment of diabetes called dipeptidyl peptidase IV (DPP-IV) inhibitors, significantly improved glycaemic control in patients with type 2 diabetes compared to placebo and exhibited a safety and tolerability profile similar to placebo. In addition, treatment with sitagliptin had no effect on body weight, was not associated with gastrointestinal (GI) related adverse events, and demonstrated a low risk of hypoglycaemia.

These data, which came from the results of two twelve-week placebo controlled Phase II studies and a small short-term Phase II study of sitagliptin in combination with metformin, were presented at the 65th annual meeting of the American Diabetes Association in San Diego.

"Results from the studies conducted to date are very promising," said John M. Amatruda, vice president, Metabolism/Clinical and Quantitative Sciences at Merck & Co., Inc. "These studies demonstrate proof of concept for sitagliptin in short-term clinical studies. Longer term trials, such as those now underway in Phase III, should provide greater insight into the efficacy, the ability to maintain glycaemic control over a longer period of time, the tolerability profile of sitagliptin, and other potential values of this treatment including its use with other oral agents."

Effect of sitagliptin on glycaemic control

Results from a 12-week, double-blind, placebo-controlled, parallel group study in patients with type 2 diabetes showed that sitagliptin significantly reduced HbA_{1c} (A1C) from baseline as compared to placebo with an average reduction of 0.6 percent observed in the sitigliptin 100 mg once daily group (p<.001).

The majority of the patients in this study had mild to moderate hyperglycaemia. The mean baseline A1C was approximately 7.7 with 28.8 percent of patients having a

baseline A1C at or less than 7.0 percent. Observed differences in A1C between patients taking sitagliptin and patients administered placebo were greatest in those patients with a higher baseline A1C at randomization. In patients with a higher A1C baseline (i.e., between 8.5 and 10 percent), a 0.8 percent reduction, relative to placebo, was seen in patients randomized to the 100 mg once daily dose of sitagliptin using data carried forward, that is including patients whether they completed the study or not. A mean 1.1 percent reduction in A1C relative to placebo was observed in patients taking sitagliptin using data from patients who completed the study as per study protocol.

In this study, 552 type 2 diabetes patients, aged 30-74 years and with an HbA1C of 5.8 – 10.4% were randomized to one of five treatment groups: Placebo; sitagliptin (25 mg, 50 mg, or 100 mg) once daily; or sitagliptin 50 mg twice daily. Treatment with sitagliptin was well tolerated and resulted in no significant weight gain or incidence of GI related adverse events. Only one adverse event of hypoglycaemia was reported in each of the four sitagliptin treatment groups, compared to no adverse events of hypoglycaemia reported in the placebo group.

Efficacy and tolerability of sitagliptin

The second study presented was a randomized, double-blind, placebo-controlled study, which evaluated the efficacy and tolerability of sitagliptin in 743 patients with type 2 diabetes. The majority of the patients in this study had mild to moderate hyperglycaemia (mean baseline A1C of 7.8 - 7.9 percent). Patients were randomized to one of six treatment groups: placebo; sitagliptin (5mg, 12.5 mg, 25 mg, or 50 mg twice daily); or the sulfonylurea, glipizide, 5 mg titrated to 20 mg. After a 12 week treatment period, sitagliptin significantly reduced A1C from baseline compared to placebo. The largest reduction in the patients treated with sitagliptin was 0.77 percent p<0.001, in the 50 mg twice-daily treatment group. Patients taking glipizide showed a 1.0 percent reduction from baseline in A1C. In the active treatment groups, placebo subtracted A1C results did not appear to reach a plateau.

Treatment with sitagliptin was generally well tolerated and, like placebo, resulted in no significant weight gain. Patients treated with glipizide had an average weight gain of 1.1 kilogram relative to placebo. Adverse event reports of hypoglycaemia were observed in 4 percent of patients taking sitagliptin, 17 percent of patients taking glipizide and 2 percent of patients taking placebo.

"The loss of efficacy with sulfonylureas is well described. Longer term studies with an appropriate once daily dose of sitagliptin will address the full efficacy and potential durability of sitagliptin versus glipizide," commented lead trialist Russell Scott MD, PhD, Professor of Medicine, Director of Diabetes and Lipid Research Group, Christchurch Hospital and School of Medicine, New Zealand.

Adding sitagliptin to ongoing metformin therapy

Also presented were results from a randomized, double-blind, placebo-controlled, four-week crossover study, which evaluated the efficacy and tolerability of sitagliptin in combination with metformin versus metformin plus placebo. In the United States, metformin is the most commonly used oral antihyperglycemic agent in patients with type 2 diabetes.¹

In this study, 28 patients with a mean baseline A1C range of 7.7 percent receiving metformin, were randomized to receive either metformin plus placebo or metformin plus sitagliptin 50 mg twice daily. At the end of the first 4-week treatment period, patients given metformin plus placebo were then given sitagliptin 50 mg and vice versa. After the first 4-week treatment, results of the 24-hour weighted mean glucose for patients taking metformin plus sitagliptin was 125 mg/dL as compared to 158 mg/dL in patients taking metformin plus placebo. This corresponds to a significant weighted mean glucose reduction of 32.9 mg/dL.

In all three studies, sitagliptin was generally well tolerated and demonstrated a safety and tolerability profile similar to placebo and/or the comparator drug. In each study, patients on sitagliptin reported no significant weight gain and no differences in GI-related adverse to the comparator treatment. A low risk of hypoglycaemia was also observed throughout the three trials.

About sitagliptin

Sitagliptin is an investigational medicine now under development by Merck & Co. for the treatment of type 2 diabetes. If approved, sitagliptin would be a member of a new class of antihyperglycaemic agents called DPP-IV inhibitors, which block the DPP-IV enzyme that normally inactivates the incretin gut hormones GLP-1 and GIP. Sitagliptin is expected to lower blood glucose levels by increasing the level of active incretin hormones which increase insulin from pancreatic beta-cells and decrease glucagon from pancreatic alpha cells in a glucose-dependent manner (when blood glucose is elevated and not when blood glucose is low).

.

¹ IMS - NPA Plus audit, as of Dec 04

About Merck

Merck & Co., Inc., which operates in many countries as Merck Sharp & Dohme, (MSD), is a global research-driven pharmaceutical company dedicated to putting patients first. Established in 1891, Merck discovers, develops, manufactures and markets vaccines and medicines in more than 20 therapeutic categories. The company devotes extensive efforts to increase access to medicines through far-reaching programs that not only donate Merck medicines but help deliver them to the people who need them. Merck also publishes unbiased health information as a not-for-profit service. For more information, visit www.merck.com.

Forwarding-Looking Statement

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995. These statements involve risks and uncertainties, which may cause results to differ materially from those set forth in the statements. The forward-looking statements may include statements regarding product development, product potential or financial performance. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. Merck undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Merck's business, particularly those mentioned in the cautionary statements in Item 1 of Merck's Form 10-K for the year ended Dec. 31, 2004, and in its periodic reports on Form 10-Q and Form 8-K, which the company incorporates by reference.