Kyowa Hakko Kirin Announces Top-Line Results of Global Phase 3 Trial of KW-6002 (Istradefylline) for Parkinson's Disease

Tokyo, Japan, December 13, 2016 --- Kyowa Hakko Kirin Co., Ltd. (Tokyo: 4151, President and CEO: Nobuo Hanai, "Kyowa Hakko Kirin") announced today that top-line results of a global Phase 3 trial of istradefylline (generic name; code name, KW-6002) did not meet its primary endpoint in patients with Parkinson's disease.

This study was to evaluate the efficacy of KW-6002 (20 mg or 40 mg once-daily treatment for 12 weeks) in patients with moderate to severe Parkinson's disease with "wearing-off phenomenon" on levodopa therapy, in comparison with placebo, and to assess the safety of both doses. A trend toward greater reduction in the daily off-time compared with placebo was observed in the 20 mg and 40 mg KW-6002 groups throughout the evaluation period. However, there was no statistically significant difference in the primary outcome measure, i.e., the change from baseline in daily off-time, at Week 12 between the 20 mg or 40 mg KW-6002 group and the placebo group. In terms of safety, KW-6002 was well tolerated at both 20 and 40 mg doses.

"The results of this global Phase 3 trial of istradefylline are not what we expected," said Yoichi Sato, Managing Executive Officer, Vice President, Head of Research and Development Division of Kyowa Hakko Kirin. "We need to fully understand the study results and will present further findings including those from the secondary outcome measures at upcoming scientific congresses and/or in scientific journals. In addition, we will pursue a chance to work with FDA and discuss potential for successful submission."

The Kyowa Hakko Kirin Group companies strive to contribute to the health and well-being of people around the world by creating new value through the pursuit of advances in life sciences and technologies.

Outline of the Global Phase 3 Trial

ClinicalTrials.gov Identifier	NCT01968031
Design	Double-blind, placebo-controlled, randomized, multinational, multicenter phase 3 study
Subjects	609 moderate to severe Parkinson's disease patients with wearing-off phenomena on levodopa therapy
Number of Sites	89 sites in eight countries
Doses and Treatment Duration	20 mg, 40 mg of istradefylline or placebo, orally once daily for 12 weeks
Primary Endpoint	Change from baseline in OFF hours per day

About Parkinson's disease

A progressive, neurodegenerative disease characterized by motor symptoms such as tremors, rigidity, slow movement and postural reflex disorders. It is thought to be caused by progressive degeneration associated with decreased levels of dopamine in certain parts of the brain, i.e., the substantia nigra and striatum.

About istradefylline

Istradefylline is a first-in-class adenosine A_{2A} receptor antagonist. Istradefylline is indicated for the improvement of the “wearing-off” phenomenon in patients with Parkinson’s disease on levodopa-containing preparations and has been marketed as the brand name NOURIAST® in Japan since May 30, 2013.

About adenosine A_{2A} receptor

Adenosine A_{2A} receptors are a G protein-coupled receptor (GPCR), and also one of the receptors of adenosine, a substance widely distributed in the human body. In the brain, adenosine A_{2A} receptors are considered to be present specifically in the basal ganglia, of which degeneration or abnormality is noted in Parkinson's disease. The basal ganglia are known to play an important role in motor control.

About levodopa

Levodopa (L-DOPA) is a standard of care drug that is most effective for the treatment of Parkinson’s disease. Long-term use of levodopa, however, is often complicated by fluctuation (e.g., wearing-off) of the effects. This study was conducted in patients with Parkinson’s disease taking levodopa plus a second anti-Parkinson's disease agent (either dopamine agonist, MAO-B inhibitor, or COMT inhibitor).