KYOWA KIRIN

News release

Kyowa Kirin Announces FDA Approval of NOURIANZ™ (istradefylline) for Use in Parkinson's Disease

First and only Adenosine A_{2A} receptor antagonist for use in Parkinson's Disease in the U.S.

Tokyo, Japan, August 28th, 2019 – Kyowa Kirin Co., Ltd., (Kyowa Kirin, TYO: 4151) announces today that the U.S. Food and Drug Administration (FDA) has granted approval for NOURIANZ™ (istradefylline) for use as adjunctive treatment to levodopa/carbidopa in adult patients with Parkinson's disease (PD) experiencing "OFF" episodes.

"We are proud that NOURIANZ is now ready to help adult patients with Parkinson's disease in the US," said Tomohiro Sudo, Head of Global Product Management Office of Kyowa Kirin, "We believe that NOURIANZ could be an important contributor to improve treatment outcomes. We will keep working to bring the product to patients globally."

"Kyowa Kirin has a commitment to global health and well-being by creating new value through the pursuit of advances in life sciences and technology particularly in oncology, nephrology, immunology, and the central nervous system," says Tom Stratford, President of Kyowa Kirin USA Holdings, Inc. "Today's FDA approval of NOURIANZ is an important milestone and provides US patients with a novel non-dopaminergic once-a-day oral treatment option to be used in conjunction with levodopa/carbidopa for Parkinson's disease."

"Today's approval is the culmination of decades of perseverance in exploring the science and clinical effects of istradefylline and inhibition of adenosine A_{2A} receptor signaling in people with Parkinson's disease," said Jeffrey S. Humphrey, MD, Chief Development Officer of Kyowa Kirin Pharmaceutical Development, Inc. "In clinical studies, istradefylline, used as adjunctive treatment to levodopa/carbidopa in adult patients with PD experiencing "OFF" episodes, was associated with a decrease in OFF Time and increase in ON Time without troublesome dyskinesia. We are grateful for the FDA approval and for the many dedicated scientists and

patients whose participation in our research programs has resulted in a new treatment option for Parkinson's disease."

"Istradefylline is an Adenosine A_{2A} receptor antagonist, and is a novel non-dopaminergic pharmacologic approach to treating OFF episodes for people living with PD," said Dr. Stuart Isaacson, MD, Parkinson's Disease and Movement Disorders Center of Boca Raton, Florida. "Based on data from four clinical studies, istradefylline taken as an adjunct to levodopa significantly improved OFF time and demonstrated a well-tolerated safety profile. Istradefylline represents an important new treatment option for patients with Parkinson's disease who experience "OFF" episodes."

The FDA approval of NOURIANZ is based on findings from randomized, multi-center, double-blind, placebo-controlled trials in patients with PD taking a stable dose of levodopa/carbidopa with or without other PD medications.

The Kyowa 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.

Please see NOURIANZ indication and Important Safety Information below.

Indication

NOURIANZ™ (istradefylline) is an adenosine receptor antagonist indicated as adjunctive treatment to levodopa/carbidopa in adult patients with Parkinson's disease (PD) experiencing "off" episodes.

Important Safety Information

Warnings and Precautions

Dyskinesia: NOURIANZ in combination with levodopa may cause dyskinesia or exacerbate pre-existing dyskinesia. In clinical trials, 1% of patients treated with either NOURIANZ 20 mg or 40 mg discontinued treatment because of dyskinesia, compared to 0% for placebo.

Hallucinations / Psychotic Behavior: Because of the potential risk of exacerbating psychosis, patients with a major psychotic disorder should not be treated with NOURIANZ. Consider dosage reduction or discontinuation if a patient develops hallucinations or psychotic behaviors

while taking NOURIANZ.

Impulse Control / Compulsive Behaviors: Patients treated with NOURIANZ and one or more medication(s) for the treatment of Parkinson's disease (including levodopa) may experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge or compulsive eating, and/or other intense urges, and the inability to control these urges. In clinical trials, 1 patient treated with NOURIANZ 40 mg was reported to have impulse control disorder, compared to no patient on NOURIANZ 20 mg or placebo.

Drug Interactions

The maximum recommended dosage in patients taking strong CYP3A4 inhibitors is 20 mg once daily. Avoid use of NOURIANZ with strong CYP3A4 inducers.

Specific Populations

Pregnancy: Based on animal data, may cause fetal harm.

Hepatic impairment: The maximum recommended dosage of NOURIANZ in patients with moderate hepatic impairment is 20 mg once daily. Avoid use in patients with severe hepatic impairment.

Adverse Reactions

The most common adverse reactions with an incidence ≥5% and occurring more frequently than with placebo were dyskinesia (15%, 17%, and 8%), dizziness (3%, 6%, and 4%), constipation (5%, 6%, and 3%), nausea (4%, 6%, and 5%), hallucination (2%, 6%, and 3%), and insomnia (1%, 6%, and 4%) for NOURIANZ 20 mg, 40 mg, and placebo, respectively.

About Kyowa Kirin

Kyowa Kirin commits to innovative drug discovery driven by state-of-the-art technologies. Kyowa Kirin focuses on creating new values in the four therapeutic areas: nephrology, oncology, immunology/allergy and neurology. Under the Kyowa Kirin brand, the employees from 36 group companies across North America, Europe and Asia/Oceania unite to champion the interests of patients and their caregivers in discovering solutions wherever there are unmet medical needs.
You can learn more about the business of Kyowa Kirin at https://www.kyowakirin.com

About NOURIANZ™ (istradefylline) tablet

NOURIANZ is an orally administered, selective adenosine A_{2A} receptor antagonist approved in the US for adjunctive treatment to levodopa/carbidopa in adult patients with Parkinson's disease (PD) experiencing "OFF" episodes. The product has been marketed in Japan under the brand name NOURIAST® since May 30, 2013. In Japan, NOURIAST® is indicated for the improvement of the

"wearing-off" phenomenon in patients with Parkinson's disease on levodopa-containing preparations.

About Parkinson's disease

Parkinson's disease is a progressive, neurodegenerative disease characterized by motor symptoms such as tremors, rigidity, slow movement and postural instability. 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.

# # #