FOR MEDICAL / TRADE MEDIA ONLY

News release

Kyowa Kirin Provides Update on Application for Marketing Authorisation of Istradefylline in Europe for the Treatment of 'OFF' Episodes in People Living with Parkinson's

TOKYO, Japan, 15 November 2021 – Kyowa Kirin Co., Ltd. (TSE:4151, President and CEO: Masashi Miyamoto, "Kyowa Kirin") today announced that following a re-examination procedure the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) issued a negative opinion for istradefylline as an add-on treatment to levodopa (L-Dopa) based regimens in adults living with Parkinson's, experiencing end-of-dose motor fluctuations. Parkinson's is a chronic, progressive neurodegenerative condition that affects small regions in the brain that control movement, balance and posture.[1] It is the fastest growing neurodegenerative disorder in the world.[2]

"We are disappointed by the CHMP opinion. We will take time to assess our plans for istradefylline in EMEA," said Tomohiro Sudo, Executive Officer, Head of Global Product Strategy Department at Kyowa Kirin. "We appreciate the collaboration we have had with all stakeholders and applaud the Parkinson's community for their commitment to supporting people living with this chronic, debilitating condition."

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. The company is committed to bringing our innovative therapies to patients.

About istradefylline

Istradefylline was developed as a novel, first-in-class non-dopaminergic, adenosine A_{2A} receptor antagonist that reduces 'OFF' time in people living with Parkinson's through selective targeting of adenosine A_{2A} receptors in the basal ganglia. Whilst dopaminergic treatment targets the dopamine receptors in the direct and indirect pathways to facilitate movement, istradefylline, as an add-on to L-Dopa, reduces the activity of the indirect pathway which suppresses movement.[3,4] Consequently, it helps restore the balance within the basal ganglia.[1,2]

About Parkinson's and 'OFF' episodes

There are an estimated 10 million people in the world currently living with Parkinson's.[5] Although it is classically characterised by motor symptoms (symptoms involving movement), people living with the condition also experience a large range of non-motor symptoms, which add to the complexity of living with the condition.[5]

Although Parkinson's is not life threatening there is currently no cure.[1] Over time symptoms progress and can be unpredictable, imposing a significant impact on daily life.[1] This impact can extend to caregivers, friends and family, whose own wellbeing and quality of life can deteriorate as a result.[6]

'OFF' episodes is used to describe the return of Parkinson's symptoms, also known as 'OFF' symptoms, and can be triggered by a variety of phenomena, including:[7]

- Delayed onset of response to medication
- Reduced duration of benefit from a medication
- Reduced or no efficacy of a dose of medication

About Kyowa Kirin

Kyowa Kirin strives to create and deliver novel medicines with life-changing value. As a Japan-based Global Specialty Pharmaceutical Company with a more than 70-year heritage, we apply cutting-edge science including an expertise in antibody research and engineering, to address the needs of patients and society across multiple therapeutic areas including Nephrology, Oncology, Immunology/Allergy and Neurology. Across our four regions – Japan, Asia Pacific, North America and EMEA/International – we focus on our purpose, to make people smile, and are united by our shared values of commitment to life, teamwork/Wa, innovation, and integrity. You can learn more about the business of Kyowa Kirin at: https://www.kyowakirin.com/.

Kyowa Kirin International is a subsidiary of Kyowa Kirin Co., Ltd.

References

1. European Parkinsons Disease Association. About Parkinson's, https://www.epda.eu.com/about-parkinsons/what-is-parkinsons/ [Last accessed Novemeber 2021].
2. Dorsey ER, Sherer T, Okun MS, et al. The Emerging Evidence of the Parkinson Pandemic. *J Parkinsons Dis* 2018; 8: S3-s8. 2018/12/26. DOI: 10.3233/jpd-181474.
3. Saki M, Yamada K, Koshimura E, et al. In vitro pharmacological profile of the A2A receptor antagonist istradefylline. *Naunyn Schmiedebergs Arch Pharmacol* 2013; 386: 963-972. 2013/07/03. DOI: 10.1007/s00210-013-0897-5.
4. LeWitt PA, Aradi SD, Hauser RA, et al. The challenge of developing adenosine A(2A) antagonists for Parkinson disease: Istradefylline, preladenant, and tozadenant. *Parkinsonism Relat Disord* 2020; 80 Suppl 1: S54-s63. 2020/12/23. DOI: 10.1016/j.parkreldis.2020.10.027.
5. Ball N, Teo W-P, Chandra S, et al. Parkinson's Disease and the Environment. *Frontiers in Neurology* 2019; 10. Mini Review. DOI: 10.3389/fneur.2019.00218.
6. Armstrong MJ, Rastgardani T, Gagliardi AR, et al. The impact of off periods on persons with Parkinson's and care partners: a

qualitative study. *Neurol Clin Pract* 2020;10.1212/CPJ.0000000000000921.

7. Freitas ME, Hess CW and Fox SH. Motor Complications of Dopaminergic Medications in Parkinson's Disease. *Semin Neurol* 2017; 37: 147-157. 2017/05/17. DOI: 10.1055/s-0037-1602423.