

News release

Kyowa Kirin Announces Positive Phase 3 Results of Tenapanor (KHK7791) for Hyperphosphatemia in Patients on Hemodialysis in Japan

Tokyo, Japan, December 13, 2021 --Kyowa Kirin Co., Ltd. (TSE:4151, President and CEO: Masashi Miyamoto, "Kyowa Kirin") announced that results of the phase 3 clinical study in Japan for tenapanor (Code name: KHK7791)^{*1}, a small molecule compound licensed from Ardelyx, Inc. (Fremont, Calif. and Waltham, Mass., USA; Nasdaq: ARDX, President and CEO: Mike Raab, "Ardelyx")^{*2}, met its primary endpoint.

The phase 3 study is a double-blind and placebo-controlled clinical study to investigate the efficacy and safety of KHK7791 (tenapanor) for 164 adult hyperphosphatemia^{*3} patients with chronic kidney disease (CKD) on hemodialysis in Japan. The primary efficacy endpoint of the study is the changes from baseline in serum phosphorous levels at week 8 after the start of the drug administration. Statistically significant decrease in serum phosphorous levels was observed in the KHK7791 group relative to the placebo group. In this study, the safety profile for tenapanor was consistent with prior studies in this patient population, with no new safety signals identified.

"We are very pleased with the positive result of this study evaluating efficacy and safety of tenapanor in hyperphosphatemia patients under maintenance dialysis," said Yoshifumi Torii, Ph.D., Executive Officer, Vice President, Head of R&D Division of Kyowa Kirin. "We will steadily advance the other three clinical studies that are currently underway and strive to deliver tenapanor with a unique mechanism of action as a novel value to patients."

Tenapanor, discovered by Ardelyx, is a first-in-class phosphate absorption inhibitor. Kyowa Kirin and Ardelyx initially established a collaboration partnership in November 2017 through a license agreement that Kyowa Kirin obtained exclusive rights to develop and commercialize tenapanor, for the treatment of cardiorenal diseases, including hyperphosphatemia, in Japan. Kyowa Kirin has conducted three phase 2 studies and is conducting the other three phase 3 studies^{*4} (Phosphate Binder-combination, Parallel-group Comparative Study, Study of KHK7791 in Hyperphosphatemia Patients on Peritoneal Dialysis and Long-term, Phosphate Binder Switch Study) in Japan.

The detailed results of the study are planned to be presented through academic conferences and publications.

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.

***1: About Tenapanor**

Tenapanor, discovered and developed by Ardelyx, is a first-in-class selective sodium–hydrogen exchanger 3 (NHE3) inhibitor. It has a unique mechanism of action that acts by blocking the NHE3 sodium transporter in the GI tract, reducing the absorption of dietary sodium and resulting in increased protons within the cells. The mechanism is different from the current standard therapy with phosphate binders. The increase in protons causes a reduction in phosphate uptake by tight junctions that regulate phosphate absorption in the GI tract. It is absorbed minimally in oral administration and has very low exposure in blood. Given that any significant changes in other ions, other than sodium have not been observed in preclinical or clinical studies, this mechanism appears to be specific to phosphate absorption overall.

***2: About Ardelyx Inc.**

Ardelyx is focused on discovering, developing and commercializing innovative first-in-class medicines to meet significant unmet medical needs. Ardelyx received approval for IBSRELA (tenapanor) with plans to launch in the second quarter of 2022. Ardelyx is developing tenapanor, a novel product candidate to control serum phosphorus in adult patients with CKD on dialysis, which has completed three successful Phase 3 trials. Ardelyx is also advancing RDX013, a potassium secretagogue, for the potential treatment of elevated serum potassium, or hyperkalemia, a problem among certain patients with kidney and/or heart disease and has an early-stage program in metabolic acidosis, a serious electrolyte disorder in patients with CKD. Ardelyx has established agreements with Kyowa Kirin in Japan, Fosun Pharma in China and Knight Therapeutics in Canada for the development and commercialization of tenapanor in their respective territories.

***3: About Hyperphosphatemia**

Hyperphosphatemia is a serious condition resulting in an abnormally elevated level of phosphorus in the blood that is estimated to affect more than 745,000 dialysis patients in major developed countries. The kidney is the organ responsible for regulating phosphorus levels, but when kidney function is significantly impaired, phosphorus is not adequately eliminated from the body. As a result, hyperphosphatemia is a nearly universal condition among people with CKD on dialysis. Despite treatment with phosphate binders (the only approved therapy for hyperphosphatemia), 77% of CKD patients on dialysis are unable to consistently maintain phosphorus levels ≤ 5.5 mg/dL over a six-month period (Spherix Global Insights: RealWorld Dynamix, Dialysis 2019). Phosphorus levels greater than 5.5 mg/dL have been shown to be an independent risk factor for cardiovascular morbidity and mortality in patients requiring dialysis (Geoffrey A. Block, et al.: JASN, 2004, 2208-2218), and internationally recognized treatment guidelines recommend lowering elevated phosphate levels toward the normal range (<4.6 mg/dL).

***4: About KHK7791's phase 3 studies in Japan**

Kyowa Kirin announced about the initiation of KHK7791's phase 3 studies in Japan on April 13, 2021. For more information, please visit

https://www.kyowakirin.com/media_center/news_releases/2021/pdf/e20210413_01.pdf