Kyowa Kirin Initiates Phase 3 Clinical Studies of Tenapanor (KHK7791) for Hyperphosphatemia in Patients on Hemodialysis and Peritoneal Dialysis in Japan

Tokyo, Japan, April 13, 2021 --Kyowa Kirin Co., Ltd. (TSE:4151, President and CEO: Masashi Miyamoto, ”Kyowa Kirin”) announced the initiation of four phase 3 clinical studies in Japan for tenapanor (Code name: KHK7791)[*1], a small molecule compound licensed from Ardelyx, Inc. (Fremont, Calif., USA; Nasdaq: ARDX, President and CEO: Mike Raab, "Ardelyx")[*2].

These phase 3 clinical studies are multi-center studies evaluating serum phosphorus in hyperphosphatemia[*3] in patients on hemodialysis and peritoneal dialysis in Japan. These studies are to evaluating the efficacy and safety of repetitive administration of tenapanor.

Yoshifumi Torii, Ph.D., Executive Officer, Vice President, Head of R&D Division of Kyowa Kirin commented, "Tenapanor is expected to be a new treatment option for hyperphosphatemia patients under maintenance dialysis as it has a distinct mechanism from the current phosphate binder therapy. We will continue to push forward with our development activities so that we can deliver benefits and smile to patients with hyperphosphatemia under maintenance dialysis in Japan.”

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 trials. Ardelyx’s new drug application (NDA) for tenapanor is currently under review by the U.S. Food and Drug Administration (FDA) for the control of serum phosphorus in adult patients with chronic kidney disease (CKD) on dialysis.

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.

<Summary of the Study>

Study Name	A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group Comparative Study of KHK7791 in Hyperphosphatemia Patients on Hemodialysis (7791-004)
Study Population	Hyperphosphatemia patients on hemodialysis
Primary Endpoint	Changes in serum phosphorous levels
Estimated Enrollment	140 participants
Estimated Study Completion Date	October 2021

Study Name	A Phase 3, Randomized, Double-blind, Placebo-controlled, Phosphate Binder-combination, Parallel-group Comparative Study of KHK7791 in Hyperphosphatemia Patients on Hemodialysis (7791-005)
Study Population	Hyperphosphatemia patients on hemodialysis, in whom the proper management of serum phosphorus levels by phosphate binders is hard to achieve
Primary Endpoint	Changes in serum phosphorous levels
Estimated Enrollment	140 participants
Estimated Study Completion Date	October 2021

Study Name	A Phase 3, Open-label, Single-arm Clinical Study of KHK7791 in Hyperphosphatemia Patients on Peritoneal Dialysis (7791-006)
Study Population	Hyperphosphatemia Patients on Peritoneal Dialysis
Primary Endpoint	Changes in serum phosphorous levels
Estimated Enrollment	40 participants
Estimated Study Completion Date	December 2021

Study Name	A Phase 3, Long-term, Phosphate Binder Switch Study of KHK7791 in Hyperphosphatemia Patients on Hemodialysis (7791-007)
Study Population	Hyperphosphatemia patients on hemodialysis
Primary Endpoint	Safety
Estimated Enrollment	200 participants

Estimated Study Completion Date	September 2022

***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. And it is absorbed minimally in oral administration. Overall, this mechanism appears to be specific to phosphate absorption given that Ardelyx has not observed any significant changes in other ions, other than sodium, in preclinical or clinical studies.

***2: About Ardelyx Inc.**

Ardelyx is focused on discovering, developing, and commercializing innovative first-in-class medicines to enhance the lives of patients with kidney and cardiorenal diseases. Ardelyx is advancing tenapanor, a novel product candidate to control serum phosphorus in adult patients with CKD on dialysis, for which the company's NDA is currently under review by the FDA, with a PDUFA date of April 29, 2021. 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. In addition, Ardelyx received FDA approval of IBSRELA® (tenapanor) on September 12, 2019. 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 (<4.6mg/dL).