# News release

## Kyowa Kirin Announces NDA Submission of Tenapanor Hydrochloride (KHK7791) for Improvement of Hyperphosphatemia in Chronic Kidney Disease Patients on Dialysis in Japan

**Tokyo, Japan,** October 28, 2022 – Kyowa Kirin Co., Ltd. (President and CEO: Masashi Miyamoto, TSE: 4151, "Kyowa Kirin") announced the submission of a New Drug Application (NDA) for tenapanor hydrochloride (Code name: KHK7791, "tenapanor") [*1], a small molecule compound licensed from Ardelyx, Inc. (Waltham, Mass., USA; Nasdaq: ARDX, President and CEO: Mike Raab, "Ardelyx") [*2] to the Japanese Ministry of Health, Labour and Welfare for improvement of hyperphosphatemia[*3] in chronic kidney disease patients on dialysis on October 28.

"We are pleased that we have submitted an NDA for tenapanor for improvement of hyperphosphatemia in chronic kidney disease patients on dialysis," said Yoshifumi Torii, Ph.D., Executive Officer, Vice President, Head of R&D Division at Kyowa Kirin. "We strongly believe that tenapanor, with its unique mechanism of action, will provide a new treatment option for the improvement of hyperphosphatemia and contribute to the benefit of patients receiving maintenance dialysis."

This NDA is supported by data from four Phase 3 clinical trials, conducted by Kyowa Kirin in Japan in patients with hyperphosphatemia on maintenance dialysis. These data demonstrated a statistically significant reduction in serum phosphorus levels, with tenapanor both as monotherapy and when added to phosphate binders for patients whose serum phosphorus levels were poorly controlled on conventional phosphate binders alone. The results of the studies undertaken by Kyowa Kirin suggest that tenapanor may also reduce the medication burden of phosphorus management utilizing conventional phosphate binders for treating hyperphosphatemia. In these studies, the safety and tolerability profile for tenapanor was consistent with prior studies in Japan, with no new safety signals identified.

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 under which Kyowa Kirin obtained exclusive rights to develop and commercialize tenapanor, for the treatment of cardiorenal diseases, including hyperphosphatemia, in Japan.

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 Hydrochloride**

Tenapanor hydrochloride (“tenapanor”), discovered and developed by Ardelyx, is a first-in-class phosphate absorption inhibitor. Tenapanor with a unique blocking mechanism of action, acts locally in the gut to inhibit the sodium hydrogen exchanger 3 (NHE3), reducing phosphate absorption through the paracellular pathway, the primary pathway of phosphate absorption.

***2: About Ardelyx Inc.**

Ardelyx was founded with a mission to discover, develop and commercialize innovative first-in-class medicines that meet significant unmet medical needs. Ardelyx’s first approved product, IBSRELA® (tenapanor) is available in the United States and Canada. Ardelyx is developing XPHOZAH® (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 has a Phase 2 potassium lowering compound, RDX013, for the potential treatment of elevated serum potassium, or hyperkalemia, a problem among certain patients with kidney and/or heart disease and 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 with internationally recognized KDIGO treatment guidelines that recommend lowering elevated phosphate levels toward the normal range (2.5-4.5mg/dL).