News release

Kyowa Kirin Announces Approval of PHOZEVEL® for Improvement of Hyperphosphatemia in Chronic Kidney Disease Patients on Dialysis in Japan

Tokyo, Japan, September 25th, 2023 –Kyowa Kirin Co., Ltd. (President and CEO: Masashi Miyamoto, TSE: 4151, "Kyowa Kirin") announced today that it has received an approval for manufacturing and marketing PHOZEVEL® (Generic name: tenapanor hydrochloride, Development code: KHK7791)[*1], a small molecule compound licensed from Ardelyx, Inc. (Waltham, Mass., USA; Nasdaq: ARDX, President and CEO: Mike Raab, "Ardelyx")[*2], for the improvement of hyperphosphatemia in chronic kidney disease patients on dialysis as of today.

"We are excited to announce the manufacturing and marketing approval of PHOZEVEL® for the 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 expect that PHOZEVEL®, with its novel mechanism of action as a phosphate absorption inhibitor, will provide a new treatment option for the improvement of hyperphosphatemia in chronic kidney disease patients on dialysis and significantly improve the quality of life for patients. We appreciate Ardelyx's continued support to bringing this drug to market. Under the continued strong partnership, we will work closely to provide appropriate product information for PHOXEVEL® to patients and healthcare professionals in Japan who are in need of a new option to manage their hyperphosphatemia"

"The approval of PHOZEVEL® in Japan marks the very first regulatory approval of tenapanor for hyperphosphatemia. I thank our partners at Kyowa Kirin for their long-standing collaboration and congratulate them for their tireless efforts to get PHOZEVEL® approved," said Mike Raab, President and CEO at Ardelyx. "Together with Kyowa Kirin, we believe PHOZEVEL® can provide a meaningful benefit for chronic kidney disease patients on dialysis. With this approval, nephrologists in Japan will now have an important novel treatment option for the management of elevated serum phosphorus levels. We look forward to continuing this important relationship and supporting Kyowa Kirin as they bring this novel product to patients and the entire Japanese kidney community."

This approval is based on the results of 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 PHOZEVEL®, 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 PHOZEVEL® may also reduce the medication burden of phosphorus management utilizing conventional phosphate binders for treating hyperphosphatemia and the long-term management of serum phosphorus levels can be maintained. In these studies, the safety and tolerability profile for PHOZEVEL® was consistent with prior studies in Japan, with no new safety signals identified.

PHOZEVEL® discovered and developed by Ardelyx in the United States, is a first-in-class phosphate absorption inhibitor. Kyowa Kirin entered into an exclusive license agreement with Ardelyx in November 2017 for the development and commercialization rights for this product in Japan, targeting cardiorenal diseases, including hyperphosphatemia.

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 PHOZEVEL® (Tenapanor Hydrochloride)**

PHOZEVEL®, discovered and developed by Ardelyx, is a first-in-class phosphate absorption inhibitor. PHOZEVEL® 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 who have an inadequate response or intolerance to phosphate binder therapy, which has completed three successful Phase 3 trials and an additional two Phase 4 open label 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. 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). Over 2 million people worldwide currently receive treatment with dialysis or a kidney transplant to stay alive, yet this number may only represent 10% of people who actually need treatment to live.[#]

Couser WG, Remuzzi G, Mendis S, Tonelli M. The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. Kidney Int. Dec 2011;80(12):1258-1270.