News release

Kyowa Kirin Announces Presentations of the Results of Phase 3 Studies of PHOZEVEL® for Patients with Hyperphosphatemia Undergoing Dialysis in Japan at the American Society of Nephrology Meeting

TOKYO, October 17, 2023 – Kyowa Kirin Co., Ltd. (TSE:4151, President and CEO: Masashi Miyamoto, "Kyowa Kirin") announces that major results of two phase 3 studies of PHOZEVEL® (Generic name: tenapanor hydrochloride, Development code: KHK7791, "tenapanor") [*1] for patients with hyperphosphatemia undergoing dialysis[*2] in Japan will be presented in two poster sessions at the American Society of Nephrology Meeting (ASN Kidney Week 2023, Philadelphia, Pennsylvania), November 2 ~ November 5, 2023. The abstracts are available on the ASN website. (https://www.asn-online.org/education/kidneyweek/)

Yoshifumi Torii, Ph.D., Executive officer, Vice President, Head of R&D Division at Kyowa Kirin commented, "We have worked closely with Ardelyx on the research and development of tenapanor, and last month, we successfully obtained approval for manufacturing and marketing of PHOZEVEL® in Japan. Through these presentations, we are pleased to share that tenapanor, as a potential treatment option for patients on hemodialysis and peritoneal dialysis with hyperphosphatemia, can significantly reduce pill burden. We believe that tenapanor to be provided as one of a convenient option for patients."

ASN Kidney Week 2023　Poster session
ID:TH-PO144
Session Date, Time: November 2, 2023 from 10:00 AM to 12:00 PM (EDT)

Title : Tenapanor effect on decrease in phosphate binder pill burden for hyperphosphatemia in Japanese patients undergoing hemodialysis: A phase 3 long-term study

Background and Method

Phosphate binders (PBs) are commonly prescribed for treating hyperphosphatemia in patients undergoing dialysis. However, management with PBs often requires a high pill burden which is

a significant medication compliance issue in patients. The ability of tenapanor to decrease PB pill burden for Japanese hemodialysis (HD) patients with hyperphosphatemia was evaluated in the long-term safety study.

This was a multicenter, open-label, single-arm, phase 3 study. HD patients whose serum phosphorus level were 3.5−7.0 mg/dL at baseline received tenapanor 5 mg BID added to their PB regimen for 52-weeks. The tenapanor dose was titrated in a stepwise manner within the range of 5, 10, 20 and 30 mg BID. The dose of tenapanor and PBs was adjusted based on serum phosphorus levels from Week 2, while controlling serum phosphorus levels and switching from PBs to tenapanor. While the primary endpoint was safety of the 52-week tenapanor treatment, the key secondary endpoint was a ≥30% reduction in the total number of daily phosphorus lowering pills, PBs plus tenapanor, from baseline.

Major Results

Overall, 212 patients participated in this study. 158 patients (77.5%) achieved a ≥30% reduction in the total daily pill number of PBs and tenapanor. Complete switching from PBs to tenapanor was achieved in 93 patients (45.6%). From Week 0 to Week 52, the mean (SD) daily pill number of PBs decreased from 11.4 (7.62) to 3.1 (5.48). Mean (SD) serum phosphorus levels were well controlled, 5.24 (0.96), 4.01 (1.14), and 5.11 (1.17) mg/dL at baseline, Week 2, and Week 52, respectively. The major drug-related adverse event was diarrhea (56.6%), and most events were mild in severity. In this study, the safety profile for tenapanor was consistent with prior studies in this patient population.

Conclusion

Tenapanor demonstrated its ability to significantly decrease the pill number of PBs and was well tolerated in the long-term administration. These results suggest that tenapanor could achieve the dual targets of controlling serum phosphorus levels and decreasing PB pill burden.

ASN Kidney Week 2023　Poster session
ID:TH-PO145
Session Date, Time: November 2, 2023 from 10:00 AM to 12:00 PM (EDT)

Title : Efficacy and safety of tenapanor in Japanese peritoneal dialysis patients with hyperphosphatemia: Results of a phase 3 study

Method

This was a multicenter, open-label, single-arm, phase 3 study in Japanese peritoneal dialysis (PD) patients with hyperphosphatemia. Patients were enrolled if serum phosphorus levels were

3.5−7.0 mg/dL at screening and elevated to 6.1−9.9 mg/dL after PB-washout. Tenapanor dose was started at 5 mg BID and titrated to a maximum of 30 mg for 16 weeks to manage serum phosphorus levels. The primary endpoint was the mean change in serum phosphorus at week 8 from baseline.

Major Results

A total of 54 patients received tenapanor. Serum phosphorus levels decreased from a baseline of 7.65 mg/dL to 6.14 mg/dL at week 8 and 5.44 mg/dL at week 16. The change in serum phosphorus at week 8 (primary endpoint) and at week 16 from baseline was −1.18 mg/dL (95% confidence interval −1.54 mg/dL, −0.81 mg/dL) and −1.65 mg/dL, respectively. The most common adverse event was diarrhea (74.1%). All were mild or moderate in severity and only three subjects (5.6%) discontinued due to diarrhea. These results were comparable to those of the phase 3 study in Japanese HD patients.

Conclusion

Tenapanor could be a new treatment option for PD patients with hyperphosphatemia as well as HD patients.

Kyowa Kirin also conducted a phase 3, randomized, double-blind, placebo-controlled, parallel-group comparative study of tenapanor in hyperphosphatemia patients on hemodialysis and a phase 3, randomized, double-blind, placebo-controlled, phosphate binder-combination, parallel-group comparative study of tenapanor in hyperphosphatemia patients on hemodialysis. The two studies' results were presented at the American Society of Nephrology Meeting last year. In this September, Kyowa Kirin received the approval for manufacturing and marketing tenapanor (PHOZEVEL®) for the improvement of hyperphosphatemia in chronic kidney disease patients on dialysis.

PHOZEVEL®, discovered and developed by Ardelyx[*3], is a first-in-class phosphate absorption inhibitor. Kyowa Kirin and Ardelyx initially established a collaborative partnership in November 2017 through a license agreement under which Kyowa Kirin obtained exclusive rights to develop and commercialize this product 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 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 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.

***3: 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 also developing XPHOZAH® (tenapanor). 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.