News release

Kyowa Kirin Announces Phase III Study Results of bardoxolone methyl (RTA 402) in Japan and Discontinuation of Development

Tokyo, Japan, May 10, 2023 --Kyowa Kirin Co., Ltd. (TSE: 4151, President and CEO: Masashi Miyamoto, “Kyowa Kirin”) announces today the discontinuation of the clinical development program for bardoxolone methyl (RTA 402), a small-molecule compound licensed from Reata Pharmaceuticals, Inc. (Plano, Texas, USA; CEO: Warren Huff, "Reata").

RTA 402 has been designated as a "SAKIGAKE Designation" program for the treatment of diabetic kidney disease by the Ministry of Health, Labor and Welfare of Japan, and Kyowa Kirin has started a Phase III clinical study for the indication (AYAME study) in Japan from May 2018. This multi-center, randomized, double-blind, placebo-controlled study is designed to assess the efficacy and safety of RTA 402 for diabetic kidney disease, and the endpoints are listed below. The Pharmaceuticals and Medical Devices Agency (PMDA) of Japan has pointed out that not only the primary and the key secondary endpoints, but also the result regarding the secondary endpoints “Time to onset ESRD*” and others should be discussed for submitting a marketing authorization application of RTA 402 for diabetic kidney disease.

[Primary endpoint]
“Time to onset a ≥ 30% decrease in eGFR* from baseline or ESRD”
[Key secondary endpoint]
“Time to onset a ≥ 40% decrease in eGFR from baseline or ESRD”
[Other secondary endpoints]
“Time to onset a ≥ 53% decrease in eGFR from baseline or ESRD”
“Time to onset ESRD”
“Change in eGFR from baseline at each evaluation time point “

Patients administered RTA 402 showed statistically significant improvement for “Time to onset a ≥ 30% decrease in eGFR from baseline or ESRD” and “Time to onset a ≥ 40%

decrease in eGFR from baseline or ESRD", thereby meeting the primary and key secondary endpoints. On the other hand, no difference in "Time to onset ESRD" between the two groups was observed. No significant safety issues were observed in the patients administered RTA 402.

As above, though improvement in eGFR was shown in the patients administered RTA 402 and the primary and secondary endpoints were met, the occurrence of ESRD was not decreased by RTA 402 administration. Based on these results, and after discussions with key opinion leaders and PMDA, Kyowa Kirin has determined that it is difficult to file an application for manufacturing and marketing approval of RTA 402 for diabetic kidney disease in Japan and decided to discontinue the development for the indication. In addition, Kyowa Kirin will withdraw the application for manufacturing and marketing approval of RTA 402 for Alport Syndrome filed in July 2021 in Japan and discontinue development for this indication. Further, Kyowa Kirin has initiated discussions with Reata to end its participation as an In-County Clinical Caretaker CCC for the clinical trials of RTA 402 for Alport Syndrome and Autosomal Dominant Polycystic Kidney Disease.

Kyowa Kirin signed a license agreement with Reata for the exclusive rights to develop and commercialize RTA 402 for renal diseases and certain other indications in Japan, China, Taiwan, South Korea, and Southeast Asian countries on December 24, 2009.

The Kyowa Kirin Group strives 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.

***About ESRD**

Abbreviation of End-stage renal disease. In this study, ESRD is defined as (1) initiation of maintenance dialysis, (2) renal transplantation, (3) sustained eGFR ≤6 ml/min/1.73 m2 for ≥4 weeks, and (4) other ESKD cases as determined by the Kidney Event Assessment Committee.

***About eGFR**

Abbreviation of estimated glomerular filtration rate. Although the inulin-clearance method, the gold standard for measuring GFR, is used in case of need for an accurate evaluation of kidney function for such as kidney transplant donor, eGFR based on the serum creatinine level is widely used to assess kidney function in clinical practice.