News release

Kyowa Kirin Announces NDA Submission of Bardoxolone Methyl (RTA 402) for Alport Syndrome in Japan

Tokyo, Japan, July 28th, 2021 – Kyowa Kirin Co., Ltd. (President and CEO: Masashi Miyamoto, Kyowa Kirin, TSE: 4151) announced that Kyowa Kirin has submitted an NDA of bardoxolone methyl (RTA 402) for the treatment of Alport Syndrome on July 27th.

Bardoxolone methyl is a small-molecular compound licensed from Reata Pharmaceuticals, Inc. (President and CEO: Warren Huff, Reata), which was designated as an orphan drug for the indication of "improvement of renal function in Alport Syndrome" by the Ministry of Health, Labour and Welfare (MHLW) on May 24th, 2021. With the designation, it is eligible for priority review.

“We are pleased that we have submitted an NDA of bardoxolone methyl for Alport Syndrome, a serious, progressive disease with an unmet need for new therapeutic options,” said Tomohiro Sudo, Executive Officer, Head of Global Product Strategy Department of Kyowa Kirin. “We strongly believe that bardoxolone methyl has the potential to deliver a meaningful therapeutic advantage to Alport Syndrome patients and their families.”

This application is based on the efficacy and safety data from the CARDINAL Phase 3 clinical trial, which was conducted by Reata for patients with Alport Syndrome. The primary efficacy endpoints of the study were the changes from baseline in estimated glomerular filtration rate (eGFR) at Week 48 and Week 100 after the start of the drug administration. At both time, significant improvements in eGFR were observed in bardoxolone methyl group relative to the placebo group.

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.

About Bardoxolone Methyl

Bardoxolone methyl is a small-molecular compound that activates nuclear factor erythroid 2-related factor 2 (Nrf2), a transcription factor that has a key role in the body’s protective response to stress. A wide range of anti-oxidative and anti-inflammatory effects of this compound could

improve kidney function. In the phase 2 clinical study conducted in Japan (TSUBAKI), administration of bardoxolone methyl resulted in a significant improvement in glomerular filtration rate (kidney function) measured using the inulin clearance method. Besides Alport Syndrome, the phase 3 study in patients with Diabetic Kidney Disease (AYAME) and the phase 3 study in patients with Autosomal Dominant Polycystic Kidney Disease (FALCON) are currently ongoing.

About Alport Syndrome

Alport Syndrome is a progressive genetic disease that causes hematuria, proteinuria and decreased renal function, and is one of the intractable diseases designated by the Ministry of Health, Labour and Welfare in Japan. Alport Syndrome is caused by genetic mutations in the type IV collagen alpha chain, a component of the glomerular basement membrane, and is a disease that often leads to a gradual decline in renal function and eventually to end-stage kidney failure. Type IV collagen is also present in the inner ear and eye, being accompanied by hearing loss and ocular abnormalities. To date, no disease-specific treatment has been established, and the main treatment is nephroprotective therapy aimed at slowing the decline in renal function.

About CARDINAL study

CARDINAL was a phase 2/3 study in patients with Alport Syndrome aged 12-70 years and with baseline eGFR of 30-90 mL/min/1.73m^2. The Phase 3 portion of CARDINAL was an international, randomized, placebo-controlled, double-blind study, and the change from baseline in eGFR was evaluated at Weeks 48, 52, 100, and 104 after the start of the drug administration.

For these endpoints, the mean values for bardoxolone methyl group were significantly higher than those for the placebo group at each time point, indicating a clinically meaningful improvement in eGFR.

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.