News release

Kyowa Kirin Announces Top-Line Results of Phase 3 Clinical Study of KW-3357 for the Treatment of Preeclampsia in Japan

Tokyo, Japan, September 28, 2023 --Kyowa Kirin Co., Ltd. (Kyowa Kirin, TSE:4151, President and CEO: Masashi Miyamoto) announced that top-line results of the phase 3 KOUNO-TORI study of KW-3357 (Generic name: Antithrombin Gamma (Genetical Recombination), Product Name: ACOALAN®) for the treatment of preeclampsia in Japan did not meet the primary endpoint.

The Phase 3 study is a multi-centered, randomized, placebo-controlled, double-blind trial conducted in Japan to access efficacy and safety of KW-3357 for patients with early onset severe preeclampsia. The primary endpoint is days of maintaining pregnancy (The period from the start of administration of the investigational drug to the end of pregnancy). A total of 183 eligible patients were enrolled in this study, and they were randomly assigned in a 1:1 ratio to the KW-3357 group and the placebo group. Out of these, 181 subjects received at least one administration of KW-3357 or physiological saline solution, with a maximum duration of 7 days.

Regarding the efficacy, there was a trend toward longer days of maintaining pregnancy in the KW-3357 group compared to the placebo group, but the difference was not significant. (Mean days of maintaining pregnancy: 16.9 days in KW-3357 group vs 13.0 days in placebo group, $p = 0.0719$)

In terms of safety, the occurrence of bleeding-related events and anemia in KW-3357 group was approximately three times higher compared to the placebo group. (Bleeding-related events occurrence: 28% in KW-3357 group, 9% in placebo group. Anemia: 27% in KW-3357 group, 10% in placebo group) Additionally, there were 3 reported cases of neonatal death in KW-3357 group. The causes of neonatal death were congenital tracheal atresia, sepsis, pulmonary alveolar haemorrhage, and the causal relationship with KW-3357 was ruled out for any of these events.

Currently the future development strategy for KW-3357 is under discussion.

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 KW-3357

KW-3357 is an antithrombin (AT) drug created through the technology of recombinant DNA and sugar-chain control, which is a recombinant AT preparation with the same amino acid sequence and the same type of sugar chain structure as human natural AT. AT inhibits blood coagulation by forming a complex with the coagulation factor of proteolytic enzyme. In Japan, KW-3357 has been approved for the treatments of thrombophilia due to congenital AT deficiency (CAD) and disseminated intravascular coagulation (DIC) since July, 2015 and commercialized under the brand name of ACOALAN®.

Kyowa Kirin and the Japan Blood Products Organization (head office: Tokyo, Japan, President and representative director: Takahide Ishikawa, "JB") have signed an outsourcing agreement concerning sales of ACOALAN® in Japan. Under the agreement, JB is responsible for the commercial activity and information providing to medical institutions.

About Preeclampsia

Preeclampsia is gestational hypertension accompanied by one or more of the following new-onset conditions at or after 20 weeks' gestation: Proteinuria, Other maternal organ dysfunction, Uteroplacental dysfunction. Severe preeclampsia can result in both acute and long-term complications for both the pregnant and her newborn. Maternal complications of severe preeclampsia include pulmonary edema, myocardial infarction, stroke, acute respiratory distress syndrome, coagulopathy, severe renal failure, and retinal injury. These complications are more likely to occur in the presence of preexistent medical disorders and with acute maternal organ dysfunction related to preeclampsia. Fetal and newborn complications of severe preeclampsia result from exposure to uteroplacental insufficiency or from preterm birth, or both.