

## Kyowa Hakko Kirin Acquired Approval for Additional Formulation of ACOALAN® in Japan

Tokyo, Japan, Sep. 14<sup>th</sup>, 2017 --- Kyowa Hakko Kirin Co., Ltd. (Tokyo: 4151, President and CEO: Nobuo Hanai, "Kyowa Hakko Kirin") announced today that additional formulation, ACOALAN® injection 1800 (generic name: Antithrombin Gamma (Genetical Recombination)) has received manufacturing and marketing approval (MMA) in Japan from the Ministry of Health, Labor and Welfare.

ACOALAN® is an antithrombin (AT) drug created through the technology of recombinant DNA and sugar-chain control. Using of ACOALAN® could avoid a risk of infection caused by human blood since ACOALAN® is a recombinant AT preparation. ACOALAN® injection 600 for thrombophilia due to congenital AT deficiency (CAD) and disseminated intravascular coagulation (DIC) has already been approved for MMA since July 3<sup>rd</sup>, 2015.

ACOALAN® injection 1800 enables expansion of ACOALAN® line-up, in which 600 international units (IU) vial only previously.

"We are pleased to announce this additional approval," said Masashi Miyamoto, PhD., Director of the Board, Managing Executive Officer, Director of Corporate Strategy & Planning Department. "We believe that the partial change and the addition of the 1800IU vial for ACOALAN® will help healthcare providers by reducing their operational burdens."

Kyowa Hakko Kirin and the Japan Blood Products Organization (head office: Tokyo, Japan, President and representative director: Takahide Ishikawa, "JB") have signed an outsourcing agreement concerning domestic sales of ACOALAN®. JB will also be responsible for selling ACOALAN® injection 1800 and providing information to medical institutions.

The Kyowa Hakko 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.

<Summary of the approval>

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| [Product Name]              | ACOALAN® injection 600, <u>ACOALAN® injection 1800</u>   |
| [Generic Name]              | Antithrombin Gamma (Genetical Recombination)   |
| [Indication]                | Thrombophilia due to congenital antithrombin deficiency (CAD)<br>Disseminated intravascular coagulation (DIC) accompanied by a decrease in antithrombin  |
| [Dosage and Administration] | The product should be reconstituted with the supplied water for injection, and the reconstituted solution should be administered either by slow intravenous injection or by intravenous infusion.<br>1. Thrombophilia due to CAD<br>The dosage is 24 to 72 IU/kg administered once daily.<br>2. DIC accompanied by a decrease in antithrombin<br>The usual adult dosage is 36 IU/kg administered once daily. The dose may be adjusted according to the patient's condition. The maximum daily dose should not exceed 72 IU/kg. |

※Underline are points related to this approval

**About Antithrombin (AT)**

AT is a serine protease inhibitor, which is a single chain glycoprotein with a molecular weight of about 60,000 produced by liver and vascular endothelial cell. AT binds to blood coagulation factors such as thrombin and activated forms of Factor X, which are serine proteases, and inhibits blood coagulation.

**About Congenital Antithrombin Deficiency (CAD)**

CAD is a genetic disorder characterized by iterative thrombosis. Continued AT deficiency results in a decrease in anticoagulant activity, and minor factors that normally would not lead to thrombus formation can result in thrombosis.

**About Disseminated Intravascular Coagulation (DIC)**

DIC may be observed as a disorder that accompanies cancer, serious infections such as septicemia, leukemia, malignant lymphoma, placental abruption and so forth. When a person has DIC, blood clots are formed more easily in the capillaries around the body and results in clots that obstruct blood circulation in organs such as the kidneys, liver, and brain, which then causes disorders in the affected organs. If many clots form, platelets and coagulant factors are spent not to form new clots for hemostasis. The reactions to dissolve clots get to be enhanced for the multiple clots at the same time. These things result in bleeding.