NEWS RELEASE

NIPPON SHINYAKU CO., LTD.

17th October, 2018

New Drug Application Filed for defibrotide sodium

Nippon Shinyaku Co., Ltd (HQ: Minami-ku, Kyoto, President: Shigenobu Maekawa) announced today that Nippon Shinyaku filed a new drug application (NDA) to the Ministry of Health, Labour and Welfare (MHLW), for defibrotide sodium (NS-73) for the treatment of hepatic veno-occlusive disease (VOD, or sinusoidal obstruction syndrome) *1 in Japan.

VOD is a known complication associated with hematopoietic stem cell transplantation (HSCT), a potential curative treatment for blood cancers. Signs of VOD include increased bilirubin levels, weight gain, hepatomegaly, ascites, and jaundice. In severe cases, VOD can cause multi-organ dysfunction or failure, leading to death in up to 80% of patients. Since no clinically useful drug is currently established in Japan, medical specialists as well as the patients have been longing for the development of a new drug over the years.

Defibrotide is a single-stranded nucleic acid polymer derived from porcine intestine mucosa and is thought to work by protecting vascular endothelium and normalizing the coagulation/fibrinolysis balance. The product is commercially available in 35 countries including the U.S. and EU as the world-first therapy for severe hepatic VOD associated with hematopoietic stem cell transplantation.

Nippon Shinyaku acquired a license of defibrotide from Jazz Pharmaceuticals plc (HQ: Dublin, Ireland, Chairman & CEO: Bruce C. Cozadd) as of March 30, 2017. Defibrotide received orphan drug designation from MHLW for the treatment of VOD following hematopoietic stem-cell transplantation on September 14, 2018. Nippon Shinyaku submitted the NDA based on the results from the Japanese investigator sponsored clinical studies and the global studies conducted by Jazz Pharmaceuticals.

Approval and launch of defibrotide would enable Nippon Shinyaku to contribute to the treatment of patients with VOD in Japan.

*1: Hepatic veno-occlusive disease is also known as sinusoidal obstruction syndrome, because hepatic sinusoid is the starting point for injury in this complication.

ABOUT JAZZ PHARMACEUTICALS PLC

Jazz Pharmaceuticals plc, established in 2003, is an international biopharmaceutical company with headquarters in Dublin, Ireland. The company is focused on the development and commercialization of products that address debilitating and life-threatening conditions with a focus in the fields of sleep and hematology/oncology. Jazz Pharmaceuticals markets mainly Xyrem® (sodium oybate) oral solution for the treatment of narcolepsy, Erwinaze® (asparaginase Erwinia chrysanthemi) for acute lymphoblastic leukemia, Defitelio® (defibrotide sodium) for the treatment of patients with VOD with renal or pulmonary dysfunction following HSCT, and Vyxeos® (cytarabine and daunorubicin liposome injection) for the treatment of high risk acute myeloid leukemia.

For more information, please visit http://www.jazzpharmaceuticals.com/.