ONO PHARMACEUTICAL CO.,LTD.

October 28, 2021

**ONO Submits an Application of ONOACT® for Intravenous Infusion 50mg/150mg, a Short-Acting Selective $\beta_1$ Blocker, in Japan for Additional Indication of Tachyarrhythmia in Pediatric Patients with Low Cardiac Function for a Partial Change in Approved Items of Manufacturing and Marketing Approval**

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") announced today that it submitted an application of ONOACT® for Intravenous Infusion 50mg/150mg (generic name: landiolol hydrochloride) ("ONOACT"), a short-acting selective $\beta_1$ blocker in Japan for additional indication of tachyarrhythmia (supraventricular tachycardia, atrial fibrillation and atrial flutter) in pediatric patients with low cardiac function for a partial change in approved items of the manufacturing and marketing approval.

This application is based on the results of a multi-center, open-label, single-arm, late Phase Ⅱ/Ⅲ study in pediatric patients with tachyarrhythmia accompanied by low cardiac function (ONO-1101-31).

In case of low cardiac function with unstable hemodynamics, such as after open-heart surgery for congenital heart diseases in pediatric patients, if tachyarrhythmia persists, it may be potentially serious or fatal. Therefore, the treatment for tachyarrhythmia is immediately required. Since non-drug treatment such as catheter ablation may be sometimes difficult in pediatric patients depending on their physique and age, drug treatment is an important and main treatment method. However, there are a few antiarrhythmic drugs approved for pediatric indications and treatment options are limited in Japan. Therefore, a new treatment option is required in this pediatric patient population.

ONOACT is a short-acting selective $\beta_1$ blocker that reduces heart rate by selectively blocking $\beta_1$ receptor which is present predominantly in the heart. ONOACT has already been approved for the treatment of tachyarrhythmia in adult patients with low cardiac function. In the results of this pediatric study, it was shown that ONOACT also lowered heart rate rapidly without reducing cardiac function. Therefore, ONOACT is expected to contribute to the treatment of tachyarrhythmia in pediatric patients with low cardiac function.

ONO received an approval of ONOACT for emergency treatment of intra-operative tachyarrhythmia (atrial fibrillation, atrial flutter and sinus tachycardia) in adult patients in July 2002 and launched it for the indication in September 2002. Then, ONO received approvals for the following additional indications in adult patients:

- Emergency measurement of post-operative tachyarrhythmia (atrial fibrillation, atrial flutter and sinus tachycardia) occurring under the monitoring of circulatory dynamics (October 2006)
- Tachyarrhythmia (atrial fibrillation and atrial flutter) in low cardiac function (November 2013)
- Life-threatening arrhythmia (ventricular fibrillation and hemodynamically unstable ventricular tachycardia) that is refractory and needs emergency measurement (March 2019)
- Tachyarrhythmia (atrial fibrillation, atrial flutter and sinus tachycardia) associated with sepsis (June 2020)

Contact
ONO PHARMACEUTICAL CO., LTD.
Corporate Communications
public_relations@ono.co.jp