## ONO PHARMACEUTICAL CO., LTD.

President and Representative Director: Gyo Sagara,

Code No.: 4528 at the 1<sup>st</sup> section of the Tokyo / Osaka Stock Exchange

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# Results of Phase II Study of ONO-2745/CNS 7056, a Short-acting General Anesthetic

Ono Pharmaceutical Co., Ltd. announced today that it has completed a phase II clinical study of ONO-2745/CNS 7056 (development code), which has been developed by PAION (formerly CeNeS) and now its development in Japan is promoted by ONO for general anesthesia. The outline of the study results are shown below.

This study was conducted in Japan as an open-label study in surgery patients undergoing general anesthesia in combination with analgesics. ONO-2745/CNS 7056 was intravenously administered to 85 surgery patients 20 years or older, with the purpose of induction of general anesthesia for 45 patients, and induction and maintenance of general anesthesia for 40 patients.

All 43 patients analyzed among the patients who received ONO-2745/CNS 7056 for induction of general anesthesia achieved loss of consciousness and underwent successful intubation, while all 32 patients analyzed among the patients who received ONO-2745/CNS 7056 for induction and maintenance of general anesthesia achieved loss of consciousness and underwent successful intubation with successful completion of a surgery without need of rescue therapy for sedative effects.

No adverse events of concern were observed. As expected in 98.8% of patients adverse events were observed due to the nature of the intervention (surgery), including primarily wound complication, laboratory test abnormal, and blood pressure decreased, which correspond with relatively common events typically observed in perioperative patients. There is no concern on safety.

ONO entered into a license agreement with PAION (formerly CeNeS) in August 2007, acquiring the exclusive rights to develop and market ONO-2745/CNS 7056 in Japan.

#### <References>

## About ONO-2745/CNS 7056

ONO-2745/CNS 7056 is an innovative short-acting benzodiazepine derivative, which binds to the binding site of the GABA receptors\*, enhancing binding of GABA to its binding site to increase function of GABA receptors, which leads to the onset of sedative effects. The results of preclinical studies showed that intravenous infusion of ONO-2745/CNS 7056 led to instant sedation, and its continuous infusion provided stable drug effects. Since it is rapidly metabolized by tissue esterase enzymes, resulting in rapid reversal of sedation after completion of treatment, ONO-2745/CNS 7056 is expected to have clinical applications for induction and maintenance of general anesthesia as well as Intensive Care Unit sedation in patients under mechanical ventilation. It also has potential as a sedative during diagnostic procedures.

#### \*GABAA receptor

GABA (gamma aminobutyric acid) is a kind of amino acid functioning as a neurotransmitter in the brain. GABA binds to GABA receptors in the cerebral cortex, cerebellum, hippocampus, and brainstem to exert sedative, hypnotic, anxiolytic, and anticonvulsant effects, inhibiting neural activity. There have been known 3 kinds of GABA receptors, GABA<sub>B</sub>, GABA<sub>B</sub>, GABA<sub>C</sub> receptors. The GABA<sub>A</sub> receptor has GABA and benzodiazepine binding sites.

## About PAION (PAION AG)

PAION is headquartered in Aachen, Germany and has a second site in Cambridge, UK. The company is specialised in developing innovative drugs for the hospital-based treatment in indications for which there is a substantial unmet medical need. PAION is extending its "Search & Develop" business model, by transforming into a "Specialty Pharma Company", with a focus on anaesthesia products.

For more information, please visit the website of PAION (<a href="http://www.paion.com/">http://www.paion.com/</a>).