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To whom it may concern,

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Announcement on Commencing Company-Supported Physician-Initiated Clinical Trials for Foramen Ovale Closure Devices

Japan Lifeline Co., Ltd. ("JLL") announced today that JLL will provide financial assistance to a company-supported physician-initiated clinical trial on a foramen ovale closure device. The clinical trial will be conducted with Dr. Teiji Akagi, Assistant Professor of the Adult Congenital Heart Disease Center of Okayama University Hospital as a coordinating investigator.

The foramen ovale is an opening in the interatrial septum, the wall separating the left and right atria. The opening is important for directing oxygen-rich blood supplied by the maternal placenta from the right atrium through the left atrium to the whole body only during fetal life, when pulmonary circulation is not possible. Usually, the foramen ovale closes spontaneously after birth but may remain unclosed in adulthood, a condition called patent foramen ovale (PFO). It has generally been reported to be present in 15-25% of healthy adults.

A number of clinical experiences have been reported that the closure of the foramen ovale with a catheter improves migraine headaches in patients with drug-resistant migraine, and a high rate of improvement in migraine has been observed after catheter closure of the foramen ovale to prevent recurrences in patients with migraine headache who developed paradoxical cerebral embolism at Okayama University Hospital.

Under these circumstances, JLL agreed with Dr. Akagi's intention to use this device in the treatment of many patients in Japan by enabling catheter therapy using a foramen ovale closure device, and decided to cooperate in a company-supported physician-initiated clinical trial in Japan.

JLL has completed consultations with Okayama University and the Pharmaceuticals and Medical Devices Agency (PMDA) regarding this clinical trial in May 2018. The company anticipates that the enrollment will start around August 2019, and that the completion of the clinical trial, including the follow-up, will be around 2023.

In addition, the PFO closure device, which is the product of Occlutech Holding AG (Switzerland) used in this study, was approved of CE mark in 2011 and is a widely used closure device in Europe. Figulla Flex II®, an atrial septal defect closure device with a structure similar to the PFO closure device, was introduced in Japan in 2016 and is now used to treat many patients.

JLL will work to establish and disseminate new treatment methods for migraine headaches through the cooperation in this clinical trial so as to provide the most up-to-date and optimal medical devices to patients and medical practice.

About migraine headaches

Today, the annual prevalence of migraine in Japan is reported to be 8.4%, of which 2.6% is referred to as migraine with aura. In some cases, there are associated symptoms such as nausea and vomiting, light, sound, odor sensitivity, and dizziness. Seventy-four percent of patients with migraine are said to have trouble with their daily activities. In addition to losing an average of 3.5 hours a week for migraine headaches, migraine patients are required to spend more than 2 million yen per year on medication and medical care. The annual health economic loss in Japan is estimated to be approximately 300 billion yen.

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