*NEWS RELEASE*

NIPPON SHINYAKU CO., LTD.

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# MHLW approval of Uptravi® for the Treatment of inoperable Chronic Thromboembolic Pulmonary Hypertension (CTEPH) or persistent/recurrent CTEPH after surgery

**KYOTO, Japan, August 25, 2021** – Nippon Shinyaku Co., LTD. (Nippon Shinyaku; Headquarters, Kyoto; President, Toru Nakai) announced that Nippon Shinyaku, which is a marketing authorization holder of Uptravi® Tablets 0.2mg and 0.4mg (Generic name: Selexipag) in Japan, has obtained approval for an additional indication of Chronic Thromboembolic Pulmonary Hypertension (CTEPH) inoperable or persistent/recurrent CTEPH after surgery from the Ministry of Health, Labor and Welfare (MHLW).

CTEPH is a disease in which thrombi form inside the pulmonary vessels (pulmonary embolism), and this causes increasing pressure on the pulmonary arteries and decreasing blood flow in the lungs and heart. Symptoms include feeling hard to breathe when moving the body or getting tired quickly. If the disease progresses, other symptoms such as swollen feet and breathing hard even after a little movement may develop due to poor heart function. The number of patients in Japan is approximately 4,200, and it is designated as an intractable disease.
Treatment consists of surgery to remove the thrombus, catheters to widen the blood vessels, or orally available medicine that opens the pulmonary arteries.

Uptravi® was designated as an orphan drug by MHLW for the indication of CTEPH in June 2016. In Japan, we have developed Uptravi® in collaboration with Janssen Pharmaceutical K.K. (Janssen Japan; HQs, Tokyo; President, Shuhei Sekiguchi).

We are dedicated to the development and commercialization of therapeutic agents and providing medical information, focusing on the field of intractable/rare diseases. We hope that we will be able to contribute to patients suffering from CTEPH, their families, and healthcare professionals as a result of the approval of this additional indication.

<About Uptravi®>

Uptravi® is an agonist which binds in a selective and long-acting manner on prostacyclin IP receptors. Uptravi® shows vasodilatory effect by acting selectively on IP receptor, and improves pulmonary hemodynamics. In Japan, it was launched in November 2016 for the oral treatment of PAH. Overseas, Janssen, a global collaborator, has received approval for Uptravi® in over 60 countries worldwide for the oral treatment of PAH. In Japan, we are promoting the provision and collection of drug information on Uptravi® in cooperation with Janssen Japan. Uptravi® has also been approved by the U.S. Food and Drug Administration (FDA) for intravenous (IV) treatment of PAH in adult patients with WHO functional class (FC) II–III, who are temporarily unable to take oral therapy.

<About prostacyclin receptor (IP receptor) agonists>

Binding of $PGI_2$ to prostacyclin (prostaglandin $I_2$/$PGI_2$) receptors in the body causes dilation of peripheral blood vessels and inhibition of platelet aggregation. $PGI_2$ receptor agonists, such as Uptravi®, are drugs that enhance these effects.

<About Orphan Drugs>

This is a medical product designated by the MHLW after reviewing on the fact that the number of patients in Japan is less than 50,000 and that it is particularly necessary for medical care.

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