PRESSRELEASE

SHIONOGI

Acceptance of a New Drug Application for Naldemedine, a Treatment for Opioid-Induced Constipation, in China

OSAKA, Japan, May 30, 2025 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") announced that the New Drug Application (NDA) for naldemedine tosilate (hereinafter "naldemedine"), a treatment for opioid-induced constipation (OIC), has been accepted in China.

Naldemedine is a peripherally acting μ-opioid receptor antagonist (PAMORA) originally developed by our company. It has been launched in countries and regions such as Japan, the United States, Europe, and Taiwan, contributing to the improvement of symptoms in many patients suffering from opioid-induced constipation (OIC).
In cancer pain management, opioid analgesics play a central role; however, their side effects can sometimes make continued treatment difficult. Among these, constipation is a common adverse effect observed in 40–80% of patients using opioid analgesics[1, 2]. It imposes a significant physical burden and greatly affects patients' quality of life (QOL), making it a major challenge in pain management[3, 4]. In China, treatment options for OIC are limited, and current approaches mainly involve symptomatic treatments such as dose adjustments of opioids or the use of laxatives[5]. Therefore, there is a strong need for new therapeutic options to achieve better pain management. The approval of naldemedine in China is expected to contribute to improving the QOL of patients suffering from OIC.

This new drug application is based on favorable results from a Phase III clinical trial[6] conducted in China targeting patients with OIC. The application was submitted through our group company, Shionogi China Co., Ltd. (Head Office: Shanghai, China; Chairman and CEO: Tatsumori Yoshida.; hereafter "SCN"), Following approval, the sales of naldemedine in China will be handled by SCN which has entered into an exclusive license agreement with Chia Tai Tianqing Pharmaceutical Group Co., Ltd. ((Head Office: Jiangsu Province, China; CEO: Eric Tse.; hereinafter "CTTQ") for the import and domestic distribution of the product[7]. CTTQ will be responsible for sales in mainland China, and our company will receive a certain amount of revenue based on sales volume.

Shionogi has identified "contributing to a healthier and more prosperous life" as a key material issue and is committed to creating a society where everyone can live longer, more vibrant lives in their own way. We will continue to contribute to improving the QOL of patients suffering from various types of pain.

About Naldemedine
Naldemedine is a peripherally acting μ-opioid receptor antagonist that binds to μ-opioid receptors in the gastrointestinal tract and counteracts the peripheral effects of opioids, thereby improving OIC. Naldemedine has been approved in countries and regions including Japan, the United States, Europe, and Taiwan. It is marketed under the brand name Symproic® in Japan, the United States, and Taiwan, and as Rizmoic® in Europe.

About Chia Tai Tianqing (CTTQ)

CTTQ is a subsidiary of China Biopharma and serves as the core pharmaceutical company of the Chia Tai Group in China. It is engaged in the integrated research, development, manufacturing, and sales of pharmaceuticals, with over 14,000 employees. The company offers a wide range of products for infectious diseases, respiratory diseases, cancer, liver diseases, endocrine disorders, and more. Over 7,000 academic and sales staff are involved in providing medical information.

Overview of the Phase III Clinical Trial in China

This Phase III clinical trial was a multicenter, randomized, double-blind, placebo-controlled study conducted in China to evaluate the efficacy and safety of naldemedine in adult patients with opioid-induced constipation (OIC) who were receiving opioid analgesic therapy.

The primary endpoint of the study was the proportion of patients who achieved three or more spontaneous bowel movements (SBMs) per week, along with an increase of at least one SBM per week from baseline.

The naldemedine treatment group demonstrated a statistically significant improvement compared to the placebo group.

Reference:

1. Droney, J. et al. : Support Care Cancer, 2008, 16 (5), 453
2. Kalso, E. et al. : Pain, 2004, 112 (3), 372
3. Abramowitz, L. et al. : J Med Econ., 2013, 16 (12), 1423
4. Bell TJ, et al. : Pain Med 10 (1), 35-42, 2009
5. Chinese Medical Association, et al. Guidelines for primary care of chronic Constipation (2019) [J]. Chinese General Practitioners Journal, 2020, 19(12): 1100–1107.
6. Chinese Clinical Trial Registry: Phase III clinical trial registration number: ChiCTR2400089290
7. Shionogi China Co., Ltd. Press release on January 2, 2025
   Ping An-Shionogi Signs an Exclusive License Agreement with Chia Tai Tianqing Pharmaceutical, a Core Enterprise of Sino Biopharmaceutical, for Import and Domestic Distribution of Naldemedine, a Therapeutic Drug for Opioid-Induced Constipation

Forward-Looking Statements

This announcement contains forward-looking statements. These statements are based on expectations in light of the information currently available, assumptions that are subject to risks and uncertainties which could cause actual results to differ materially from these statements. Risks and uncertainties include general domestic and international economic conditions such as general industry and market conditions, and changes of interest rate and currency exchange rate. These risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, completion and discontinuation of clinical trials; obtaining regulatory approvals; claims and concerns about product safety and efficacy; technological advances; adverse outcome of important litigation; domestic and foreign healthcare reforms and changes of laws and regulations. Also for existing products, there are manufacturing and marketing risks, which include, but are not limited to, inability to build production capacity to meet demand, lack of availability of raw materials and entry of competitive products. The company disclaims any intention or obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise.

For Further Information, Contact:

SHIONOGI Website Inquiry Form: https://www.shionogi.com/global/en/contact.html