May 18, 2026
J-Pharma Co., Ltd.

J-Pharma Announces jRCT Registration of an Investigator-Initiated Trial of *Nanvuranlat* in Combination with Immune Checkpoint Inhibitors for Biliary Tract Cancer
— Toward Combination Therapy with Immune Checkpoint Inhibitors in First-Line Treatment for Biliary Tract Cancer —

J-Pharma Co., Ltd. today announced that information on an investigator-initiated clinical trial, JON-2404-B, has been registered and published on the Japan Registry of Clinical Trials (jRCT) in preparation for the initiation of the trial. The trial will evaluate *nanvuranlat* in combination with immune checkpoint inhibitors (ICIs) as first-line therapy for biliary tract cancer.

URL: https://jrct.mhlw.go.jp/en-latest-detail/jRCT2031260086

The trial will be conducted as an investigator-initiated clinical trial. Under an agreement with The Cancer Institute Hospital of the Japanese Foundation for Cancer Research, J-Pharma will provide support to facilitate the conduct of the trial.

Dr. Masato Osaka, Director, Department of Hepatobiliary and Pancreatic Oncology at The Cancer Institute Hospital of the Japanese Foundation for Cancer Research, the lead study site for the trial, commented as follows:

“Although the current standard treatment for biliary tract cancer is combination therapy with cisplatin/gemcitabine and anti-PD-1/PD-L1 antibodies, the 24-month survival rate remains below 25%, indicating a significant unmet medical need. In particular, after 25 weeks of treatment, therapy transitions to maintenance treatment with either anti-PD-L1 antibody monotherapy or anti-PD-1 antibody combined with gemcitabine. However, disease progression during the maintenance phase remains a major challenge. Many patients with biliary tract cancer are elderly, and even when treatment is effective, adverse events often prevent continued intensive drug therapy. Therefore, there is a need for treatment options that enable long-term continuation of standard therapy.
In this study, nanvuranlat is expected to further improve therapeutic efficacy without competing with the current standard treatment by being added to maintenance therapy from Week 19 through Week 25 and beyond after treatment initiation, in addition to the standard treatment of anti-PD-L1 antibody plus chemotherapy.”

J-Pharma's President, Masuhiro Yoshitake, commented as follows:

"Cancer cells are known to take up amino acids via LAT1, thereby acquiring the nutrients required for proliferation. It has also been reported that amino acid uptake by cancer cells may lead to amino acid depletion in the tumor microenvironment, resulting in impaired immune cell function and suppression of immune responses against cancer cells.
Nanvuranlat, a LAT1 inhibitor, not only suppresses the supply of amino acids to cancer cells but may also affect immune responses in the tumor microenvironment. Through our research, we have obtained preclinical data suggesting activation of immune cells via LAT1 inhibition. In addition, synergistic effects of *nanvuranlat* in combination with immune checkpoint inhibitors have been reported in animal models. Accordingly, this combination may represent a novel therapeutic approach through both direct effects on cancer cells and modulation of antitumor immune responses."
J-Pharma will continue to steadily advance the ongoing global Phase III clinical trial of its LAT1 inhibitor *nanvuranlat* in the United States, known as Beacon-BTC. In Japan, J-Pharma will provide support to facilitate the investigator-initiated clinical trial evaluating *nanvuranlat* in combination with an immune checkpoint inhibitor, while fully dedicating its efforts to the development of innovative medicines that bring hope to patients around the world.

About *Nanvuranlat*
Nanvuranlat (development code: JPH203) is a LAT1-selective inhibitor originally discovered and developed by J-Pharma. It is a small-molecule compound that is being clinically developed as the world's first drug candidate with this mechanism of action. LAT1 (L-type amino acid transporter 1) is a transporter involved in the cellular uptake of amino acids and is known to be highly expressed in many cancer cells. If approved as a pharmaceutical product, *nanvuranlat* has the potential to become a first-in-class drug, meaning the first approved drug with a novel mechanism of action for the treatment of the disease.

Since 2015, J-Pharma conducted a Phase I clinical trial in patients with multiple solid tumors, and based on the results of this trial, identified the potential of *nanvuranlat* for the treatment of advanced biliary tract cancer. In 2018, J-Pharma initiated a Phase II clinical trial in patients with advanced biliary tract cancer and confirmed that *nanvuranlat* demonstrated meaningful clinical efficacy as monotherapy.

In April 2022, *nanvuranlat* was granted orphan drug designation by the U.S. Food and Drug Administration (FDA). In addition, on September 25, 2024, the FDA accepted the Investigational New

Drug (IND) application for a clinical trial of *nanvuranlat* in patients with cancer. Furthermore, in May 2025, J-Pharma confirmed that the CMC (Chemistry, Manufacturing, and Controls) for commercial-scale manufacturing met the quality standards required by the FDA. Based on these developments, J-Pharma initiated a global Phase III clinical trial in December 2025.

Publication of the results of the Japanese Phase II clinical study of *Nanvuranlat*:
Furuse et al. A Phase II Placebo-Controlled Study of the Effect and Safety of *Nanvuranlat* in Patients with Advanced Biliary Tract Cancers Previously Treated by Systemic Chemotherapy. Clin Cancer Res. 2024; 30(18):3990–3995.

Preclinical Combination Effects of *Nanvuranlat* (JPH203) and Immune Checkpoint Inhibitors (ICIs)
The effects of combining *nanvuranlat* and ICI antibodies were evaluated in a 4T1 syngeneic mouse xenograft model that is resistant to cancer immunotherapy. As a result, combination treatment with nanvuranlat and ICI antibodies demonstrated a significant enhancement of antitumor activity compared with either monotherapy.
In addition, combination treatment increased CD4+ and CD8+ tumor-infiltrating lymphocytes (TILs) and reduced FoxP3-positive CD4+ T cells, which are involved in the suppression of antitumor immunity [1, 2, 3].
Furthermore, an increase in the M1/M2 macrophage ratio and suppression of cancer-associated fibroblasts (CAFs) accumulation were also observed [3], suggesting that the combination of nanvuranlat and ICI antibodies may improve the tumor immune microenvironment.

1. Zhao Y et al. Targeting LAT1 with JPH203 to reduce TNBC proliferation and reshape suppressive immune microenvironment by blocking essential amino acid uptake. Amino Acids. 2025, 57(1):27. https://doi.org/10.1007/s00726-025-03456-3
2. Huang R et al. Targeting glutamine metabolic reprogramming of SLC7A5 enhances the efficacy of anti-PD-1 in triple-negative breast cancer. Front Immunol. 2023, 14:1251643. https://doi.org/10.3389/fimmu.2023.1251643
3. Nanvuranlat Investigator's Brochure version 10.0, September 2025

About J-Pharma Co., Ltd.
J-Pharma Co., Ltd. aims to pursue new possibilities for SLC transporters and contribute to the hope and health of people worldwide through the development of innovative new drugs that address unmet medical needs. Under this mission, J-Pharma has focused on LAT1 (L-type amino acid transporter 1), one of the SLC transporters discovered by the company's founder, and is advancing the development of LAT1 inhibitors to address the needs of patients with cancer and autoimmune diseases for which significant unmet medical needs remain.

For more information, please visit: https://www.j-pharma.com/en/

Inquiries:

J-Pharma Co., Ltd.
Planning Department
TEL: +81-3-6432-4270
https://www.j-pharma.com/en/contact