July 23, 2026

J-Pharma Co., Ltd.

J-Pharma Announces First Patient Dosed in Investigator-Initiated Trial Evaluating LAT1 Inhibitor *Nanvuranlat* in Combination with ICIs in First-Line Biliary Tract Cancer

J-Pharma Co., Ltd. (Head Office: Minato-ku, Tokyo; hereinafter "J-Pharma" or the "Company") today announced that the first patient has been dosed in an investigator-initiated clinical trial (JON-2404-B) evaluating *nanvuranlat* in combination with immune checkpoint inhibitors (ICIs) in the first-line treatment setting for biliary tract cancer (BTC).

This trial is designed to evaluate the clinical development potential of *nanvuranlat* in biliary tract cancer beyond the second-line setting being investigated in the ongoing global Phase III trial (Beacon-BTC), by extending its evaluation to maintenance therapy after first-line treatment. The dosing of the first patient marks the start of actual patient enrollment and treatment in this investigator-initiated clinical trial and represents an important milestone toward further patient enrollment and the evaluation of its safety and tolerability.

The trial is currently being conducted at four institutions in Japan: The Cancer Institute Hospital of JFCR, National Cancer Center Hospital, National Cancer Center Hospital East, and Kanagawa Cancer Center. Under its agreement with The Cancer Institute Hospital of JFCR, J-Pharma will support the smooth conduct of the study.

Significance of the Trial in the Development of *Nanvuranlat*

Nanvuranlat is a potential first-in-class LAT1 inhibitor that suppresses the supply of amino acids to cancer cells, thereby inhibiting their growth. Clinical benefit has been observed in a Phase II clinical trial conducted in Japan. In addition, non-clinical studies have suggested that *nanvuranlat* may affect the tumor immune microenvironment and enhance the ability of immune cells to attack cancer cells. Preclinical animal studies have also suggested that combination therapy with ICIs, which release the immune brakes imposed by cancer cells, may enhance antitumor activity.

In recent years, combination treatment with chemotherapy and immune checkpoint inhibitors has become a standard option in first-line treatment for biliary tract cancer. In this trial, *nanvuranlat* will be administered to patients who transition to maintenance therapy with an immune checkpoint inhibitor from Week 19 to Week 25 onward after initiating the current standard treatment regimen consisting of an anti-PD-L1 antibody plus chemotherapy. The trial will evaluate the safety and

tolerability of adding *nanvuranlat* in this setting. In addition to the second-line biliary tract cancer setting in which the Company is currently conducting a global Phase III trial, J-Pharma will use this trial to evaluate the development potential of *nanvuranlat* in the first-line setting, with the aim of expanding the potential indications and enhancing the business value of this product candidate.

Intellectual Property Supporting the Combination Therapy

J-Pharma holds method-of-use patent rights relating to combination therapy with *nanvuranlat* and an anti-PD-1 antibody or anti-PD-L1 antibody. The Company believes that these patent rights, together with other related patents, constitute important intellectual property supporting the competitive advantage and business value of this combination therapy. By evaluating the development potential of the combination therapy based on these patents, the Company believes that this trial may help expand future business development options.

Significance of the New Administration Method Adopted in This Trial

In this trial, *nanvuranlat* will be administered by 46-hour continuous intravenous infusion, and its safety and tolerability will be evaluated in combination with immune checkpoint inhibitors. The 46-hour continuous infusion regimen is designed to ensure adequate drug exposure. Compared with the previous administration method, this regimen may reduce the frequency of hospital visits and the burden associated with treatment administration at medical institutions, and is expected to be easier to implement in diverse clinical settings, including those outside Japan.

Development Status of *Nanvuranlat*

Following the dosing of the first patient in the global Phase III Beacon-BTC trial for biliary tract cancer in May 2026, J-Pharma has now also achieved first-patient dosing in this investigator-initiated clinical trial. These milestones represent steady progress in the development program for *nanvuranlat*. J-Pharma will continue to advance both the global Phase III clinical trial (Beacon-BTC), while providing the necessary support and cooperation to facilitate the smooth conduct of this investigator-initiated clinical trial. Through the research and development of *nanvuranlat*, a LAT1 inhibitor, the Company aims to create new treatment options. As a global drug discovery venture originating in Japan, J-Pharma will continue striving to deliver medicines that address unmet medical needs to patients around the world.

About *Nanvuranlat*

Nanvuranlat (development code: JPH203) is a novel LAT1-selective inhibitor originally discovered by J-Pharma and is the first small-molecule compound of its kind to be clinically developed worldwide. LAT1 (L-type amino acid transporter 1) is one of the transporters involved in cellular amino acid

uptake and is known to be highly expressed in many cancer cells. If approved as a pharmaceutical product, it has the potential to become a first-in-class drug with a novel mechanism of action for its target disease.

Since 2015, J-Pharma has conducted Phase I clinical studies in multiple solid tumors and identified its potential for the treatment of advanced biliary tract cancer. A Phase II clinical study targeting advanced biliary tract cancer was conducted starting in 2018, demonstrating that *nanvuranlat* monotherapy provides clinically meaningful benefit.*

Nanvuranlat was designated as an orphan drug by the U.S. Food and Drug Administration (FDA) in April 2022. Furthermore, on September 25, 2024, the Investigational New Drug (IND) application for clinical studies in cancer patients was accepted by the FDA. In addition, in May 2025, J-Pharma confirmed that the Chemistry, Manufacturing, and Controls (CMC) at the commercial manufacturing scale meet the quality standards required by the FDA. Based on these developments, the Company initiated a global Phase III clinical trial in December 2025.

* Publication on the results of the Japan 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. https://doi.org/10.1158/1078-0432.CCR-24-0461

Non-Clinical Combination Effects of *Nanvuranlat* (JPH203) and Immune Checkpoint Inhibitors (ICIs)

The combination effects of *nanvuranlat* and ICI antibodies were evaluated in a 4T1 syngeneic mouse xenograft model, which is resistant to cancer immunotherapy. The results showed that combination treatment with *nanvuranlat* and ICI antibodies significantly enhanced antitumor activity compared with each monotherapy.

The combination also increased CD4+ and CD8+ tumor-infiltrating lymphocytes (TILs) and reduced FoxP3-positive CD4+ T cells, which are involved in suppression of antitumor immunity [1, 2, 3].

In addition, an increase in the M1/M2 macrophage ratio and suppression of cancer-associated fibroblast (CAF) accumulation were 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.

Related Information

- Details of this investigator-initiated clinical trial (jRCT)
  https://jrct.mhlw.go.jp/latest-detail/jRCT2031260086
- *Nanvuranlat* and biliary tract cancer
  https://www.j-pharma.com/en/pipeline/biliary_tract_cancer/
- Global Phase III trial (Beacon-BTC) for biliary tract cancer
  https://www.j-pharma.com/en/clinical_trial/biliary_tract_cancer_p3/
- *Nanvuranlat* mechanism of action video
  https://www.j-pharma.com/assets/video/251209_EN.mp4

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, the Company 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, where existing drugs are insufficient.

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

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