January 8, 2025
Tochigi Cancer Center
J-Pharma Co., Ltd.

Tochigi Cancer Center and J-Pharma Enter Into Research Agreement Initiation of Collaborative Research on the Relationship Between the Efficacy of Nanvuranlat and Genetic Mutations in Biliary Tract Cancer Cells

Tochigi Cancer Center (Location: Utsunomiya City, Tochigi Prefecture; President: Iwao Ozawa), a local incorporated administrative agency, and J-Pharma Co., Ltd. (Headquarters: Yokohama City, Kanagawa Prefecture; CEO: Masuhiro Yoshitake) have announced the signing of a research agreement. The collaboration focuses on studying the relationship between driver gene mutations and the efficacy of nanvuranlat, an amino acid transporter LAT1 inhibitor, using biliary tract cancer cell lines. This translational research aims to pave the way for the clinical development of new treatment options for biliary tract cancer.

Dr. Hidenori Ojima, Deputy Director of Tochigi Cancer Center Research Institute and Head of the Molecular Pathology Department, commented on the significance of this research as follows:

"The options for anticancer drugs in biliary tract cancer are extremely limited and have yet to yield satisfactory outcomes. The development of even one additional effective drug would broaden treatment choices and be immensely beneficial for patients suffering from bile duct cancer. While this drug has already undergone clinical trials with promising results. It is critically important to deepen our understanding of specific genetic mutations that may lead to even higher treatment efficacy.

Leveraging the experience we have accumulated in biliary tract cancer research, we will collaborate with J-Pharma Co., Ltd. to conduct translational research aimed at delivering this novel anticancer drug as swiftly as possible to patients in need. This aligns with the mission of Tochigi Cancer Center Research Institute and represents an initiative of profound significance."

About Biliary Tract Cancer

Bile, which aids in the digestion of food, is produced in the liver. Biliary tract cancer often takes the form of a highly malignant tumor that occurs in the pathways through which bile flows (intrahepatic bile ducts, extrahepatic bile ducts, and ampulla of Vater) as well as in the gallbladder, which temporarily stores and concentrates bile.

The bile ducts are anatomically closely related to critical organs like the liver and pancreas. Consequently, as the disease progresses, these organs often become sites of tumor invasion and growth, making diagnosis and treatment increasingly challenging.
According to the latest statistics from the National Cancer Center Japan, over 21,000 people are diagnosed annually with extrahepatic bile duct and gallbladder cancers alone. The five-year

survival rate is second only to pancreatic cancer in its poor prognosis. The only curative treatment is surgical resection, but many cases are diagnosed at an advanced stage, rendering surgical resection unfeasible.

Even when surgical resection is performed, recurrence is common. For patients with unresectable biliary tract cancer or those who experience recurrence post-surgery, standard treatments such as combination therapy with gemcitabine and cisplatin or S-1 are used.

Although a few effective drugs have gradually become available for cases where standard treatment proves ineffective, they have yet to meet the expectations of patients or clinicians. Therefore, the urgent need is for the development of effective new anticancer drugs, as many as possible, and as quickly as possible

About Nanvuranlat
Nanvuranlat is a novel small-molecule compound independently discovered by J-Pharma that selectively inhibits LAT1. Since 2015, J-Pharma has conducted Phase I clinical trials targeting multiple solid tumors and identified its potential in treating bile duct cancer. From 2018, the Company carried out a Japan based Phase 2 trial over three and a half years, targeting advanced bile duct cancer, and demonstrated significant clinical efficacy as a monotherapy.

Nanvuranlat is the first compound in the world targeting LAT1 in clinical development, and if approved as a pharmaceutical product, it will be a first-in-class drug, offering a groundbreaking mechanism of action for the disease. Nanvuranlat was designated as an Orphan Drug by the U.S. Food and Drug Administration (FDA) in April 2022. This designation grants several benefits, including consultation for clinical development programs, tax credits for clinical trial costs, exemption from application fees, and seven years of market exclusivity in the United States.

On September 25, 2024, the FDA approved the Investigational New Drug (IND) application for nanvuranlat for cancer patients, and the Company is continuing discussions with the FDA in preparation for a Phase 3 trial in the U.S. slated for 2025.

*Publication on the results of the nanvuranlat Phase 2 study in Japan
Furuse et al. A Phase 2 Placebo-Controlled Study of the Effect and Safety of nanvuranlat in Patients with Advanced Biliary Tract Cancers Previously Clin Cancer Res. 2024; 30(18):3990-3995.

About Amino Acid Transporters
Many cells take in various substances to maintain their activity as nutrients. Amino acids and sugars are particularly important. Amino acid transporters play a role in transporting amino acids into the cells.

About LAT1
LAT1 (L-type amino acid transporter; gene code: SLC7A5) was discovered by Dr. Hitoshi Endou, the founder of J-Pharma, in 1998, making it the world's first discovery. LAT1 is upregulated in the cell membrane when a cell becomes cancerous and attempts to proliferate rapidly. This

results in the excessive uptake of amino acids, which serve as an energy source, leading to explosive cell growth. Recent scientific advances have provided a more detailed understanding of LAT1, and its complex molecular structure has been reported, making it an increasingly important drug target in cancer therapy. Studies have shown that cancer patients with high LAT1 expression tend to have poorer prognosis compared to those with low LAT1 expression.

1. Häfliger P, et al. Int. J. Mol. Sci. 2019; 20 (10): 2428
2. Kanai Y. Pharmacol Ther. 2022; 230:107964.
3. Otani R, et al. Cancers (Basel) 2023; 15: 1383

About Tochigi Cancer Center
Tochigi Cancer Center is a specialized cancer hospital with 291 beds. It has been designated by the Ministry of Health, Labour and Welfare as a regional cancer treatment cooperation center. The center is actively engaged in promoting cancer measures in Tochigi Prefecture by collaborating with hospitals and related organizations within the region. Its activities include training medical professionals, establishing cooperative frameworks with local medical institutions, and providing support for cancer patients.

About J-Pharma Co., Ltd.
J-Pharma Co., Ltd. aims to "pursue new possibilities for SLC transporters and contribute to the health and hope 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), 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. Currently, J-Pharma is conducting clinical development for LAT1 inhibitors such as "nanvuranlat" and "JPH034," and is also advancing research on new candidate compounds. In October 2023, the Company established a U.S. subsidiary and is closely collaborating with involved organizations and U.S. consultants to develop appropriate regulatory, development, and intellectual property strategies.
For more information about J-Pharma Inc., please visit https://www.j-pharma.com/.

For further information, please contact:

Tochigi Cancer Center Research Institute
TEL: 028-658-5151 (main)
Mail: tcc-press@tochigi-cc.jp

J-Pharma Co., Ltd.,
Administration Department, Public Relations
TEL：045-506-1155
Mail: info@j-pharma.com