J-PHARMA INC.

Front-runner in drug development on inhibitors of L-type amino acid transporter (LAT1) for treating advanced refractory cancers and autoimmune diseases

Leading Venture Plaza 1 75-1
Onocho, Tsurumi-ku,
Yokohama, Kanagawa
230-0046 Japan

Founded in 2005
Founder: ENDOU Hitoshi, MD., Ph.D.
President & CEO: YOSHITAKE Max
No. of employees: 18
Type of Ownership: Private
Primary stock exchange: N/A

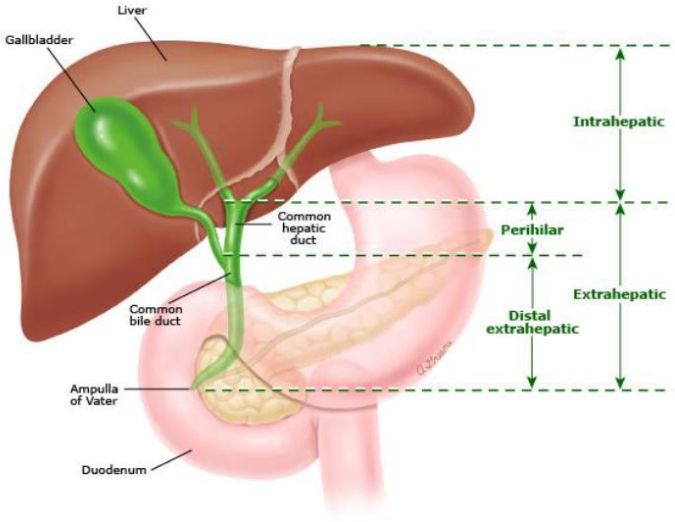
May 2023: Focusing on LAT1, discovered by the company founder as a drug target, J-Pharma's first-in-class LAT1 inhibitor nanvuranlat (development code: JPH203) for advanced refractory biliary tract cancer is on the way to the final clinical study phase.

Venture Valuation (VV) interviewed Mr. YOSHITAKE Max, President & CEO.

VV: **Biliary tract cancer is frequently diagnosed when it is already advanced. Existing drugs show little success. LAT1 inhibitor nanvuranlat, a unique small molecule compound, is expected to give hope to patients in advanced stage of all four subtypes of biliary tract cancer. No current drug candidate is efficacious for all four subtypes.**

Yoshitake: Amino acids are fundamentally vital for cancer cell proliferation. Their uptake across the cell membrane is tightly controlled by membrane transporters. L-type amino acid transporter LAT1 is one of them and has been recurrently observed overexpressed in various severe late stage cancers.

Biliary tract cancer, a rare and aggressive disease, is composed of four subtypes: intrahepatic, extrahepatic, Gallbladder, and Ampulla of Vater.



We estimate around 400,000 people are diagnosed globally with biliary tract cancer. The incidence of metastatic biliary tract cancer in the

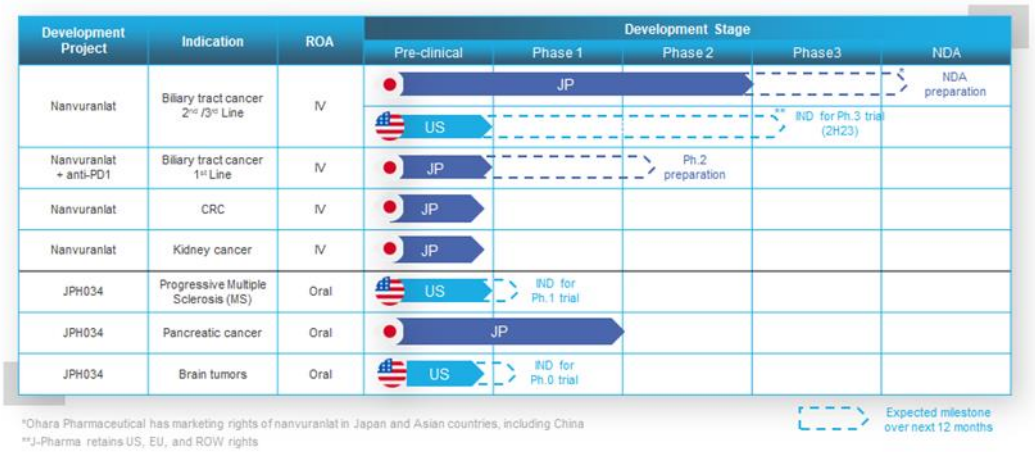
U.S., U.K., Japan and four major European countries is around 60,000 patients. The five-year survival rate is approximately 2%.

During phase II clinical study, nanvuranlat significantly improved progression-free survival over placebo in heavily pretreated patients suffering from all four areas of biliary tract cancer. Progression-free survival means that patients in late stage live with cancer but do not get worse.

The topline results were presented last January at the 2023 ASCO (American Society of Clinical Oncology) Gastrointestinal Cancers Symposium in San Francisco. The final results will be presented as an oral presentation at the 2023 ASCO Annual Meeting in June. Nanvuranlat has demonstrated proof of concept and LAT1 is regarded as a new treatment option.

VV: **In April 2022 nanvuranlat was granted orphan drug designation for the treatment of biliary tract cancer by the U.S. Food and Drug Administration (FDA). Your projects in pipeline are therefore going on in both the U.S. and Japan.**

Yoshitake: Orphan drug designation supports research into cures for rare diseases like biliary tract cancer. It allows us to receive a seven-year window of exclusive marketing rights in the U.S. upon regulatory approval, advisory consultation for clinical development programs, reduction in certain application fees, and a partial federal tax credit for clinical trial costs in the U. S.



We are taking advantage of this orphan drug status to advance our clinical studies and make nanvuranlat available to patients in the U.S. When applying for IND (Investigational New Drug) we will request a fast track designation and a breakthrough therapy designation, both of which provides for an accelerated approval process and priority review.

In Japan we are discussing with PDMA (Pharmaceuticals and Medical devices Agency) filing an NDA (New Drug Application) with phase II clinical study results.

While nanvuranlat is our top priority, we are also developing another LAT1 inhibitor, JPH034, for progressive multiple sclerosis, pancreatic cancer, brain tumors and also solid tumors.

VV: **You are preparing a clinical protocol in order to discuss with the FDA a multi-regional phase III clinical study of nanvuranlat for treatment of advanced refractory biliary tract cancer.**

Yoshitake: This multi-center, double-blind, placebo-controlled study will be performed at over 50 sites in 10 countries (US, EU and Asia). Based on the results of phase II, we will design an adaptive phase III clinical study. More specifically, we will classify the BTC patient population by biomarker and subtype. At the interim analysis, the futility will discontinue the patient enrollment in certain sub-groups. And then, the statistical power will be recalculated, and premature termination based on the interim results will be also included. Primary endpoint is progression free survival (PFS) and secondary endpoints are overall survival and disease control rate.

VV: **Having proven LAT1 as a drug target and published the chemical structure of nanvuranlat, you are accelerating the process of regulatory approval and commercialization before followers emerge. Your strategy is to self-finance the above phase III international clinical study by attracting international institutional investors via equity private placement.**

Yoshitake: Our analysis of potential global sales of nanvuranlat for biliary tract cancer identified the total value could reach $1billion. Instead of licensing out now, FDA-approved nanvuranlat will be advantageously better valued for licensing negotiation.

As a clinical stage biotech company, we are continuously considering fund raising opportunities. In particular, to fund the phase III international clinical study, which we expect to span 10 countries and have over 250 patients, we are currently considering a private placement targeting international institutional investors together with a U.S. investment bank that has extensive experience in the biopharma industry.

VV Comments after the interview:

LAT1 is one of over 400 solute carrier transporters superfamily which are expressed on the cell membrane and mediate diverse biological functions in the human body. Although they are crucial targets for drug development, they have been underexplored compared to other target genes such as GPCRs, ion channels, and kinase.

J-Pharma is the global leader in drug discovery specialized in solute carrier transporters. Some world experts have already mentioned in 2019 the outstanding efficacy of nanvuranlat (JPH203) in a published article, "The L-Type Amino Acid Transporter LAT1 – An Emerging Target in Cancer" [1].

The paper concludes that "...Of particular interest are the promising results observed with JPH203 (nanvuranlat) in a recent Phase 1 clinical trial, in which JPH203 was effective against biliary tract cancer."

Contact **Mariko Hirano,** m.hirano (at) venturevaluation.com

Venture Valuation specializes in independent assessment and valuation of technology-driven companies in growth industries, such as the Life Sciences (Biotech, Pharma, and Medtech), ICT, Femtech, Nanotech, Cleantech and Renewable Energy. In addition to valuation products, Venture Valuation offers high-quality, focused information services like the Global Life Sciences Database, Biotechgate.com and this "*Let's Interview Series*" with companies with interesting technologies and services. We select and interview thriving companies and organizations especially in Switzerland and Japan.

[1] https://pubmed.ncbi.nlm.nih.gov/31100853/