Genoscience Pharma announces launch of phase 2b clinical trial of ezurpimtrostat to treat hepatocarcinoma in combination with an immune checkpoint inhibitor and an antiangiogenic agent

- **First patient received initial treatment on January 2**
- **Addition of ezurpimtrostat to standard first-line treatment makes it possible to sensitize tumor to activity of immune checkpoint inhibitors**
- **First-line trial for treatment of hepatocellular carcinoma marks a turning point in development of Genoscience Pharma**

Marseille, France, January 6, 2023 – Genoscience Pharma, a clinical-stage biotech company developing unique lysosomotropic drug candidates for the treatment of cancer, fibrosis and auto-immune diseases through autophagy modulation, along with trial sponsor Grenoble University Hospital, today announce the launch of the ABE-LIVER study. This phase 2b clinical trial will focus on first-line treatment of HepatoCellular Carcinoma (HCC) patients with Genoscience Pharma's drug candidate ezurpimtrostat (GNS561). This is administered in conjunction with standard atezolizumab/bevacizumab treatment. The first patient received the initial treatment on January 2. Genoscience Pharma is providing ezurpimtrostat and operational support.

Although standard treatment with atezolizumab (an anti-PDL1) / bevacizumab (an antiangiogenic agent) does produce some encouraging results, a tumor response is observed in only 30% of patients and the Progression-Free Survival (PFS) period remains short. Not only does ezurpimtrostat demonstrate intrinsic anti-tumor activity, but its addition to standard treatment also allows regulation of autophagy, a key mechanism involved in immune evasion in the case of immunotherapy.

"This trial is an important step both for Genoscience and for our product ezurpimtrostat, giving us an opportunity to demonstrate the efficacy of autophagy inhibition in oncology," said Professor Philippe Halfon, CEO of Genoscience Pharma. "We have high expectations for this trial, and we are delighted to be collaborating with Grenoble University Hospital, an institution involved in a number of major clinical trials in oncology, specifically promoting ABE-LIVER, thanks to its active network in the area of liver cancer."

ABE-LIVER is a multicenter, prospective, comparative, randomized and open phase 2b trial. The principal investigator is Dr. Gaël Roth, digestive oncologist and expert in primitive hepatic tumors at the Grenoble Alpes University Hospital (CHUGA). The main objective of this trial is to evaluate the efficacy of ezurpimtrostat in conjunction with standard treatment (atezolizumab-bevacizumab) compared to standard treatment alone, as the first-line treatment in patients fighting advanced HCC. The primary criteria is PFS. Between 187 and 196 patients will be enrolled in this trial, which will take place in two stages: a preliminary safety phase involving 3–12 patients, followed by an expansion phase.

"Ezurpimtrostat could become a new weapon in our arsenal of treatments for a form of cancer that is still extremely aggressive and for which current treatments are only able to achieve a low five-year survival rate," said Professor Eric Raymond, medical director of Genoscience Pharma and head of medical oncology at the St-Joseph Hospital in Paris. "We are very optimistic and hope that by using an autophagy blocker we will be able to enhance the activity of immune checkpoint inhibitors. For patients, this means that the current treatments will become more effective."

"By targeting PPT-1, ezurpimtrostat exerts an anti-tumor effect by reducing the nutrient intake of tumor cells and sensitizes the tumor to immunotherapy by enhancing the expression of the Major Histocompatibility Complex (MHC-I) on the surface of the tumor cells. It also makes it possible to modulate the immune response through recolonization and activation of the CD8+ cytotoxic T-cells, rendering it a highly promising treatment strategy," added principal investigator Dr. Gaël Roth. "We are thrilled to have been able to start this trial, which involves most of the specialist liver cancer

centers in France. We are looking forward to evaluating the potential clinical impact of ezurpimtrostat in combination with atezolizumab-bevacizumab in HCC patients, whose treatment options are limited and whose prognosis remains very bleak at present."

The NCT05448677 trial is set to take place over three years, with intermediate results expected in 2024.

About HepatoCellular Carcinoma - HCC
With more than 900,000 new cases diagnosed each year, hepatocellular carcinoma is the fifth most common cancer in the world. Globally, it is the third most common cause of cancer-related deaths, responsible for around 830,000 deaths per year. Most hepatocellular carcinomas are not detected until they have reached an advanced stage. New treatment options are desperately needed for these patients. Hepatocellular carcinoma is the most common form of liver cancer, representing more than 75–85% of cases globally.

About ezurpimtrostat (GNS561)
Ezurpimtrostat is a human autophagy inhibitor whose activity is linked to the inhibition of PPT-1 (*Palmitoyl Protein Thioesterase-1*). Both *in vitro* and *in vivo* studies have found evidence of its high degree of tropism in the liver and powerful anti-tumor activity. Preliminary data from a phase 1b trial on primary and secondary liver tumors has confirmed that administration of ezurpimtrostat as a monotherapy is both feasible and well tolerated.

About Genoscience Pharma
Genoscience Pharma is a French clinical-stage biotechnology company developing novel lysosomotropic treatments to establish a new standard of care in cancer, fibrosis and autoimmune diseases. Its lead candidate GNS561/ezurpimtrostat is a best-in-class drug candidate that has entered phase 2b clinical trials and works by attacking cancer cells through autophagy modulation. Genoscience Pharma is developing other molecules in its portfolio for use in oncology and fibrosis indications.
www.genosciencepharma.com

Forward-looking statements
This press release may involve and contain forward-looking statements by the company about its product candidate GNS561, including its potential benefits. Such statements are based upon the current beliefs and expectations of Genoscience Pharma's management and are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, but are not limited to: additional financing, the company's ability to implement its chosen strategy, dependence upon third parties, other risks and uncertainties inherent in research and development, including the possibility of unfavorable study results, changes in the competitive environment, changes in regulations, clinical or industrial risks and all risks linked to the company's growth. There are no guarantees that future clinical trials will be completed or successful or that any Genoscience Pharma therapeutics will receive regulatory approval for any indication or prove to be commercially successful. While those factors presented here are considered representative, no such list should be considered a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof; Genoscience Pharma does not undertake any obligation to update such statements to reflect subsequent events or circumstances.

Genoscience contact
Agnes Menut
a.menut@genosciencepharma.com
FR: +33 (0)6 16 50 00 77

Press and analyst contacts
Andrew Lloyd & Associates

Saffiyah Khalique / Emilie Chouinard
saffiyah@ala.associates / emilie@ala.associates
UK: +44 1273 952 481
@ALA_Group