Genoscience Pharma completes successful phase 1b trial evaluating GNS561, PPT-1 inhibitor, in patients with primary and secondary liver cancer

- **Company identified recommended phase 2 dose for continued clinical development of GNS561 in patients with hepatocarcinoma and other cancers**
- **Based on preclinical and clinical phase 1 data, GNS561 is moving forward in phase 2/3 studies in hepatocarcinoma in combination with immune checkpoint inhibitors, in patients where standard of care failed or was stopped for safety reason**
- **Genoscience Pharma is in ongoing discussion with potential partners regarding patient enrollment in 2021**

Marseille, France, November 18, 2020 – Genoscience Pharma, a clinical stage biotechnology company developing unique lysosomotropic drug candidates for the treatment of cancer, auto-immune and infectious diseases through autophagy modulation, announces today the successful completion of a phase 1b clinical study with GNS561, its lead candidate, in primary and secondary liver cancer patients. The company is planning to start phase 2 trials in 2021.

"Safety and biomarker data from the GNS561 phase 1b study in primary and secondary liver cancers support moving the drug into later stage clinical studies with the aim of addressing patients with liver cancer that have a fatal progression," said Thomas Decaens, M.D., chief hepato-gastroenterologist & oncologist and investigator in the GNS561 phase 1 trial at Grenoble-Alpes Centre Hospitalier Universitaire (France).

A recommended phase 2 dose has been selected and validated by the Safety Monitoring Committee (SMC). Genoscience Pharma plans to conduct a phase 2 study using GNS561 as a monotherapy. In parallel, Genoscience Pharma is planning to conduct combination trials with immune checkpoint inhibitors. It has been shown that autophagy is a key mechanism implicated in the immune evasion of immune checkpoint inhibitor therapies. By combining both treatments, in addition to its own anti-tumor activity, GNS561 has been shown to sensitize the tumor to immune checkpoint inhibitors in preclinical models.

"This is a major step for Genoscience Pharma. We are looking forward to continuing our drug development work in liver cancers and broadening the current treatment options. Data from our completed phase 1b study encourages us to pursue our efforts to treat patients that have no other satisfactory therapeutic options," said Philippe Halfon, M.D., CEO and founder of Genoscience Pharma.

Phase 1b results:
The study,which took place in the US and several European countries, enrolled 26 patients in six cohorts: 50mg, 100mg, 200mg, 400mg (three times per week), and 200mg and 300mg twice-daily. The primary objective of the trial was to assess the safety of GNS561 in patients with locally advanced or metastatic hepatocellular carcinoma (HCC) that is not deemed appropriate for a curative therapy, in patients with locally advanced or metastatic intrahepatic cholangiocarcinoma (iCCA), in patients with pancreatic adenocarcinoma (PDAC) and liver metastasis, and in patients with colorectal cancer (CRC) and liver metastasis. All patients were previously exposed to one or more anti-tumor therapies (to which they were found to be refractory or intolerant).
Secondary objectives of the study were to identify the recommended phase 2 dose (RD) and to characterize the pharmacokinetics. Some exploratory objectives were evaluated such as pharmacodynamics (PD) biomarker expression in blood and in liver biopsy.

Safety data: Analysis of all the safety data to date demonstrates that GNS561 has generally been well-tolerated with no dose-limiting toxicities or unexpected safety signals. The most frequent adverse events observed are manageable gastro-intestinal events, as determined by the SMC.

Pharmacokinetics: The data observed on day one of each cycle shows an absorption profile typical of an oral administration. A long half-life has been measured and linear pharmacokinetics. As expected, there was a higher concentration of GNS561 in the liver than in the plasma.

Preliminary disease stabilization: While the phase 1b trial was a safety trial and not intended to demonstrate efficacy, the investigator-assessed best response (RECIST v1.1) to GNS561 across all cohorts supports promising clinical activity. All patients were advanced; almost half of the total number treated and 60% of HCC enrolled patients were previously exposed to three lines or more of anti-cancer therapies. A disease stabilization was observed in three patients (two in seven evaluable HCC patients and one iCCA patient).

"We are investigating all the data obtained from this phase 1 and some of the trends observed are interesting. Disease stabilization observed is a starting point, we look forward to seeing the potential of the compound in a dedicated efficacy trial. The team is writing an article to describe more of the phase 1b results we obtained; we will publish soon," said Eric Raymond, M.D., chief medical officer of Genoscience Pharma.

About GNS561
GNS561 is a PPT-1 (Palmitoyl Protein Thioesterase-1) inhibitor that blocks autophagy. Autophagy is activated in tumor cells in response to certain conditions, due to a tumor cell growth in advanced cancers. By entering the lysosomes and binding to its target, GNS561 has an important inhibiting activity on late stage autophagy, which leads to tumor cell death.

About Genoscience Pharma
Genoscience Pharma is a French clinical-stage biotechnology company developing novel lysosomotropic therapeutics to establish a new standard of care against cancer, autoimmune and infectious diseases. Its lead candidate GNS561 is a phase 2 ready best-in-class drug candidate, tackling cancer cells through autophagy modulation. Genoscience Pharma is also entering a phase 2 trial to fight Covid-19.
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 to be 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.

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