PRESS RELEASE

GENFIT: Positive Phase 1b Data with GNS561 in Combination Therapy in Heavily Pretreated Patients with Cholangiocarcinoma

- **Investigational drug GNS561 showed a favorable safety and tolerability profile in a Phase 1b study evaluating its potential in combination with a MEK inhibitor (MEKi)**
- **Study conducted in a heavily pretreated, high-unmet-need population of KRAS-mutated cholangiocarcinoma (CCA) patients who had progressed after one or two failed lines of prior standard-of-care therapy**
- **Phase 2 initiation on track for initiation in 2H26**

Lille (France), Cambridge (Massachusetts, United States), Zurich (Switzerland), June 23, 2026 - **GENFIT (Euronext: GNFT)**, a biopharmaceutical company dedicated to improving the lives of patients with rare and life-threatening liver diseases, today announced positive Phase 1b results for GNS561 in combination therapy in patients with heavily pretreated cholangiocarcinoma, demonstrating a favorable safety and tolerability profile and early signs of antitumor activity.

Clinical trial context and objective

CCA is a rare and aggressive bile duct cancer, often diagnosed at an advanced stage. It is associated with a high unmet medical need, driven by limited treatment options and poor prognosis. GNS561 is an investigational small molecule targeting PPT1, leading to autophagy inhibition and lysosomal dysfunction, thereby disrupting cancer cell survival mechanisms. By blocking autophagy, GNS561 aims to promote cancer cell death and may enhance sensitivity to other treatments. Its combination with a MEK inhibitor is intended to unlock synergistic potential by simultaneously targeting autophagy and MAPK signaling pathways. In the Phase 1b study, patients with advanced KRAS mutated CCA, who have previously failed one or two lines of prior standard of care therapies, were enrolled to evaluate the safety and tolerability of GNS561 when given in combination with trametinib, a MEKi.

Clinical results and next steps

The initial part of the Phase 1b study has been completed as planned, with 19 patients enrolled across four cohorts evaluating increasing doses of GNS561. A favorable safety and tolerability profile was observed, with no dose-limiting toxicities (DLT) reported, supporting continued clinical development. Continued signals of antitumor activity were also noted in this heavily pretreated population, with approximately half of patients achieving Stable Disease (SD) at Week 6, including one patient maintaining this status up to Week 30. While based on a limited dataset, these findings contribute to shaping the emerging clinical profile of the combination. On this basis, GENFIT has

GENFIT
TOWARDS BETTER MEDICINE

PRESS RELEASE

decided to expand the Phase 1b study with additional cohorts at higher dose levels. This expansion, intended to further strengthen the clinical dataset, does not alter the planned transition to Phase 2, which remains on track for initiation in the second half of 2026. The recommended Phase 2 dose and study design are expected to be finalized over the summer.

Dr. Mark Yarchoan, Associate Professor of Oncology at Johns Hopkins Medicine (Baltimore, MD, USA), principal investigator of the program, commented: *"Advanced KRAS-mutated cholangiocarcinoma remains an area of high unmet medical need, particularly in patients who have progressed after prior therapies. What is notable in these data is the consistency of the signal as additional patients have been treated, which helps reinforce the initial findings. Combined with a favorable safety and tolerability profile and signs of activity, these results support continued clinical investigation of this combination strategy targeting autophagy and MAPK signaling pathways."*

Details available on ClinicalTrials.gov (NCT05874414) cover both the Phase 1b and planned Phase 2 components of this open-label, multicenter study, and will be updated upon initiation of Phase 2.

END

ABOUT CHOLANGIOCARCINOMA

Biliary tract cancer (BTC) is the second most common primary liver malignancy diagnosed globally. Cholangiocarcinoma (CCA) is a type of BTC and represents approximately 15% of all primary liver tumors and 3% of gastrointestinal cancers. Based on its anatomical origin, CCA is best classified anatomically as intrahepatic (iCCA) or extrahepatic (eCCA), which is comprised of perihilar (pCCA) and distal (dCCA) CCA. Early diagnosis is a major challenge as most patients with early-stage disease do not have symptoms due to limited biliary obstruction. Rather, patients characteristically manifest symptoms related to their underlying cirrhosis, a condition present in some patients with CCA. Taken together, the majority of patients with CCA are diagnosed with advanced disease, often precluding potentially curative therapies. There are limited therapeutic options for this aggressive disease. The 5-year survival rates drop to 5-15% in the advanced and unresectable settings. The only potentially curative treatment remains surgical resection. Unfortunately, at the time of first diagnosis, only about 25% of the patients are eligible for surgery. Moreover, even after curative intent surgery, the clinical outcomes are disappointing, with 5-year survival rates of 7% to 20%.

PRESS RELEASE

ABOUT GNS561

GNS561 is a first-in-class investigational lysosomotropic agent with a novel mechanism of action. When combined with Mitogen-Activated Protein Kinase Kinase (MEK) inhibitors, GNS561 targets complementary pathways critical for cancer cell survival and proliferation, resulting in potent antitumor activity. The combination is being developed as a potential breakthrough therapy for patients with advanced solid tumors. In December 2021, we licensed the exclusive rights from Genoscience Pharma to develop and commercialize the investigational treatment GNS561 in CCA in the United States, Canada and Europe, including the United Kingdom and Switzerland. In early 2025, GENFIT completed the acquisition of the full intellectual property rights for GNS561 from Genoscience Pharma, expanding upon the limited rights initially obtained through the 2021 license.

ABOUT GENFIT

GENFIT is a biopharmaceutical company committed to improving the lives of patients with rare, life-threatening liver diseases whose medical needs remain largely unmet. GENFIT is a pioneer in liver disease research and development with a rich history and a solid scientific heritage spanning more than two decades. Today, GENFIT focuses on Acute on-chronic Liver Failure (ACLF) and associated conditions such as acute decompensation (AD) and hepatic encephalopathy (HE). It develops therapeutic assets which have complementary mechanisms of action, selected to address key pathophysiological pathways. GENFIT also targets other serious diseases, such as cholangiocarcinoma (CCA), urea cycle disorders (UCD) and organic acidemia (OA). Its R&D portfolio, covering several stages of development, ensures a constant news flow. GENFIT's expertise in developing high-potential molecules – from early to advanced pre-commercialization stages – culminated in 2024 with the accelerated approval of Iqirvo® (elafibranor) by the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom for second-line treatment of Primary Biliary Cholangitis (PBC). Iqirvo® is now marketed in several countries.[1] Beyond therapies, GENFIT also has a diagnostic franchise including NIS2+® for the detection of Metabolic dysfunction-associated steatohepatitis (MASH, formerly known as NASH for non-alcoholic steatohepatitis). GENFIT, a BCorp™ certified company since 2025, is headquartered in Lille, France and has offices in Paris (France), Zurich (Switzerland) and Cambridge, MA (USA). The Company is listed on the Euronext regulated market in Paris, Compartment B (Euronext: GNFT). In 2021, Ipsen

[1] Elafibranor is marketed and commercialized, notably in the U.S and Europe, by Ipsen under the trademark Iqirvo®

became one of GENFIT's largest shareholders, acquiring an 8% stake in the Company's capital. www.genfit.com

FORWARD LOOKING STATEMENTS

This press release contains certain forward-looking statements with respect to GENFIT, including, but not limited to, statements regarding the potential of GNS561 in combination with a MEK inhibitor in patients with cholangiocarcinoma; the safety, tolerability, activity, clinical profile and potential therapeutic benefit of GNS561; the continued development and expansion of the Phase 1b study, including additional cohorts at higher dose levels; the planned transition to, design and timing of, the Phase 2 study. The use of certain words, such as "believe", "potential", "expect", “target”, “may”, “will”, "should", "could", "if" and similar expressions, is intended to identify forward-looking statements. Although the Company believes its expectations are based on the current expectations and reasonable assumptions of the Company’s management, these forward-looking statements are subject to numerous known and unknown risks and uncertainties, which could cause actual results to differ materially from those expressed in, or implied or projected by, the forward-looking statements. These risks and uncertainties include, among others, the uncertainties inherent in research and development, including in relation to non-clinical and pre-clinical programs, reproducibility of preclinical results, the translation of animal model data to human biology, in relation to safety of drug candidates, cost of, progression of, and results from, our ongoing and planned clinical trials, patient recruitment, review and approvals by regulatory authorities in the United States, Europe and worldwide, of our drug and diagnostic candidates, pricing, approval and commercial success of elafibranor in the relevant jurisdictions, exchange rate fluctuations, and our continued ability to raise capital to fund our development, as well as those risks and uncertainties discussed or identified in the Company’s public filings with the AMF, including those listed in Chapter 2 "Risk Factors and Internal Control" of the Company's 2025 Universal Registration Document filed on April 3, 2026 (no. 26-0221) with the Autorité des marchés financiers ("AMF"), which is available on GENFIT's website (www.genfit.fr) and the AMF's website (www.amf.org), and those discussed in reports filed with the AMF or otherwise made public, by the Company. In addition, even if the results, performance, financial position and liquidity of the Company and the development of the industry in which it operates are consistent with such forward-looking statements, they may not be predictive of results or developments in future periods. These forward-looking statements speak only as of the date of publication of this press release. Other than as required by applicable law, the Company does not undertake any obligation to update or revise any forward-looking information or statements, whether as a result of new information, future events or otherwise.

PRESS RELEASE

CONTACTS

GENFIT | Investors

Jean-Christophe Marcoux – Chief Corporate Affairs Officer | Tel: +33 3 2016 4000 | jean-christophe.marcoux@genfit.com

GENFIT | Media

Bruno ARABIAN – Agence Maarc | Tel : 06 87 88 47 26 | bruno.arabian@maarc.fr

Stephanie Boyer – Press relations | Tel: +333 2016 4000 | stephanie.boyer@genfit.com