GenFleet Therapeutics (Shanghai) Inc.
勁方醫藥科技(上海)股份有限公司

(A joint stock company incorporated in the People's Republic of China with limited liability)

(Stock Code: 2595)

VOLUNTARY ANNOUNCEMENT

GFH375 Advances into A Novel Phase II Study Featuring Two First-in-world Combination Therapies for Pancreatic Cancer, including the Regimens of RAS-Targeted Inhibitor Plus Cachexia Bispecific Antibody and a Combination of Dual RAS Inhibitors Built on Distinct Mechanisms of Action

This announcement is made by GenFleet Therapeutics (Shanghai) Inc. (the "**Company**" or "**GenFleet**", together with its subsidiaries, the "**Group**") on a voluntary basis to inform the shareholders and potential investors of the Company about the latest business updates of the Group.

The board of directors of the Company (the "**Board**") is pleased to announce the initiation of a three-arm, parallel-controlled phase II study evaluating two novel combination regimens versus monotherapy of GFH375, an oral KRAS G12D (ON/OFF) inhibitor, among pretreated KRAS G12D-mutant patients with locally advanced unresectable or metastatic pancreatic cancer. The multicenter, open-label, randomized controlled study will be conducted across tens of clinical sites in the Chinese mainland; with Ruijin Hospital Affiliated to Shanghai Jiao Tong University's School of Medicine（上海交通大學醫學院附屬瑞金醫院）as the leading site. The two combination therapies include GFH375 plus GFS202A, the world's first cachexia-targeted bispecific antibody (GDF15/IL-6 bispecific antibody), and GFH375 plus GFH276, a Pan RAS (ON) inhibitor. GFH375/VS-7375 received China's first Breakthrough Therapy Designation for monotherapy in KRAS G12D-mutant metastatic pancreatic cancer in February 2026, following Fast Track designation from the U.S. FDA for KRAS G12D-mutant metastatic pancreatic ductal adenocarcinoma (PDAC) granted in 2025.

KRAS G12D mutations occur in approximately 40% of pancreatic cancer patients, while cachexia complicates cases in over 60% of this population, representing the highest cachexia prevalence among all malignancies. A recent *Nature* report delineates the treatment landscape for pancreatic cancer patients with cachexia and cited data from the multinational cachexia research initiative of CANCAN (Cancer Cachexia Action Network, co-founded by the U.S. National Cancer Institute

& Cancer Research UK). The program has enrolled nearly 1,000 cancer patients in an observational study. The publication verifies the correlation in-between heightened GDF15 concentration, tumor burden and cachexia onset, and draws upon numerous preclinical investigations showing that the increase in GDF15 level mediates pathological interaction between tumor lesions, immune system and the brain, ultimately triggering symptoms including body weight loss and diminished treatment tolerability. Separately, mice models demonstrated that elevated IL-6 level hinders dopamine secretion, which inhibits food intake and behavioral motivation.

Clinical evidence generated from overseas trials evaluating GDF15- or IL-6-targeted monoclonal antibodies paired with standard-of-care therapy for PDAC, demonstrated notable improvements in patients' physical condition and treatment tolerability, or enhanced antitumor activity alongside prolonged overall survival. Combination regimens pairing a KRAS G12D inhibitor with cachexia-targeting therapy are accordingly anticipated to deliver mechanistic synergy. GFH375 is the world's first oral KRAS G12D inhibitor that advanced into a registrational phase III monotherapy trial for metastatic pancreatic cancer. Additionally, preliminary clinical data of GFS202A was released in poster presentation at 2026 ASCO Annual Meeting, showing a favorable safety profile and encouraging therapeutic activity, with improvements in appetite, and dose-dependent increase in body weight and skeletal muscle volume.

In parallel, combining selective and Pan RAS inhibitors may elicit deeper, longer-lasting tumor response and postpone the onset of therapeutic resistance. Preclinical research by GenFleet's R&D team in KRAS G12D-mutant PDAC animal models showed that the GFH375 plus GFH276 combination yielded synergy with improved antitumor activity over single-agent treatments. Revolution Medicines, an overseas developer of RAS-targeted therapeutics, has started the combinational study of molecular-glue KRAS G12D inhibitor (RMC-9805) plus Pan RAS inhibitor (RMC-6236) in PDAC; preliminary data presented at 2026 ESMO GI congress suggested better objective response rate over either monotherapy.

As the world's first KRAS G12D inhibitor that entered a registrational phase III monotherapy study in pancreatic cancer, GFH375 was developed via the switch-II pocket (SIIP) binding mechanism; the SIIP mechanism also constitutes the structural basis for the commercialized KRAS G12C inhibitor fulzerasib in the Company's pipeline. GFH276 is a molecular-glue Pan RAS inhibitor with mono trial data demonstrating a favorable safety profile and preliminary efficacy consistent with its preclinical findings. Unlike the combination of two RAS inhibitors built on identical mechanisms, the Company's regimen that pairs RAS inhibitors with distinct mechanisms of action will enable dose optimization of the Pan RAS inhibitor to alleviate adverse events including rash, potentially delivering more favorable safety window and enhanced antitumor activity in treating pancreatic cancer. Additionally, data from preclinical research by GenFleet's partner Verastem Oncology showed the combination of GFH375/VS-7375 with RMC-6236 yielded more sustained tumor regression than pairing RMC-6236 with RMC-9805 in animal models.

“Given the vast unmet needs in targeted therapy for pancreatic cancer, GenFleet is committed to delivering both small-molecule and biologics monotherapies while continuously advancing innovative combination strategies to achieve synergistic efficacy and extend overall survival. We hope the world’s first combination of a RAS-targeted agent plus cachexia bispecific antibody for pancreatic cancer can resolve the challenges in treatment tolerability and therapeutic efficacy stemming from physical deterioration among patients with advanced pancreatic cancer. GFH375 and GFH276 are structurally distinct with different mechanisms of action, and we anticipate their combination may avoid overlapping toxicities and outperform doublets of RAS-targeting agents with identical mechanisms.” stated Dr. Yu Wang, Chief Medical Officer of GenFleet.

This phase II study is designed to enroll patients who have experienced disease progression or intolerance following at least one prior systemic therapy. The randomized controlled portion of the study will assess antitumor activity, safety and/or cachexia-related symptom improvements for each combination versus GFH375 monotherapy. In October 2025, GFH375 already entered a phase Ib/II study including two combinations among KRAS G12D-mutant solid tumors; one regimen combines GFH375 with standard-of-care AG chemotherapy (nab-paclitaxel and gemcitabine) in first-line PDAC, and the other with cetuximab in colorectal cancer (CRC) or PDAC.

About GFH375/VS-7375, GFS202A and GFH276

GFH375 is an orally active, potent, highly selective small-molecule KRAS G12D (ON/OFF) inhibitor designed to bind to the protein of KRAS G12D non-covalently, thereby disrupting the activation of downstream pathways and effectively inhibiting tumor cell proliferation. Preclinical studies demonstrated dose-dependent inhibition in models bearing KRAS G12D mutation; GFH375 also demonstrated low off-target risk in kinase selectivity and safety target assays. GenFleet entered into a discovery and development collaboration with Verastem to advance three novel oncology discovery programs related to RAS/MAPK pathway-driven cancers. The collaboration provides Verastem with an exclusive option to obtain a license for each of the three compounds in the collaboration after the successful completion of pre-determined milestones in a Phase I trial. Verastem selected GFH375/VS-7375, an oral KRAS G12D (ON/OFF) inhibitor, as its lead program from the collaboration in December 2023 and the license for GFH375 that was exercised in January 2025 is the first one from this collaboration. The licenses would give Verastem development and commercialization rights outside of China while GenFleet would retain rights inside of China.

GFS202A, as the world’s first bispecific antibody for cachexia, entered clinical stage in 2025. In preclinical research of GFS202A (a GDF15/IL-6 bispecific antibody), body weight, adipose tissue and muscle mass increase dose-dependently in animal models; additionally, GFS202A effectively reduces C-reactive protein levels and alleviates inflammatory responses. According to poster presentation in 2025 AACR annual meeting, comparative analysis demonstrated similar efficacy between GFS202A and ponsegromab (a GDF15 antibody) in restoring body weight, muscle, and fat mass at equimolar doses. Notably, GFS202A exhibited greater CRP reduction at lower dosage

than ponsegromab. Cachexia is a frequent complication of chronic diseases, and GFS202A holds the potential to serve as a therapeutic option for cachexia associated with heart failure, chronic obstructive pulmonary disease (COPD), chronic kidney disease, etc.

GFH276 is an oral novel small-molecule Pan RAS (ON) inhibitor hijacking Cyp A to target active, GTP bound RAS proteins of most wild/mutant subtypes, including most commonly found KRAS mutant (G12C, G12D, G12V, etc.) proteins. Preclinical research of GFH276 demonstrates dose-dependent anti-tumor activity and drives tumor regression in multiple KRAS mutant tumor models. GFH276 also holds the potential to outperform the mainstream SIIP (switch II pocket)-based KRAS inhibitors in overcoming adaptive and acquired resistance.

Forward-looking Statements

Specific information in this announcement may contain or constitute forward-looking words that are not historical facts. They can be identified by using forward-looking terminology, such as “predict”, “believe”, “plan”, “forecast”, “expect”, “will”, “may”, “should” and other words of similar meanings. Based on the management’s current beliefs, plans, estimates and expectations of the Company’s operation and market trends subject to changes beyond control, the forward-looking terminology reflects the Company’s beliefs, plans, estimates and expectations of future development. Actual outcome in the future may differ significantly from forward-looking words owing to market, policy, and R&D uncertainties, among others. Subject to the above-mentioned uncertainties, the Company makes no expressed or implied guarantee as to the accuracy, completeness or feasibility of this presentation, and you are cautioned not to solely rely on such forward-looking words. Neither the company nor any of its directors, officers, employees, shareholders, agents, related parties, consultants or representatives will be liable to you or any other person for consequences resulting from using this presentation. Investors are advised to exercise due diligence with reference to the company’s official disclosures for decision-making.

GLOSSARY OF TECHNICAL TERMS

“AACR”	American Association for Cancer Research
“AG”	Albumin-bound paclitaxel (nab-paclitaxel) + Gemcitabine
“CRC”	colorectal cancer
“CRP”	C-reactive protein
“FDA”	Food and Drug Administration
“GDF15”	growth differentiation factor-15

"HRAS"	Harvey RAS, a member of the RAS family proteins
"IL-6"	interleukin-6
"KRAS"	Kirsten RAS, a member of the RAS family proteins
"LBA"	late-breaking abstract
"MAPK"	mitogen-activated protein kinase, a family of proteins involved in transmitting signals from cell surface receptors to the nucleus
"NRAS"	neuroblastoma RAS, a member of the RAS family proteins
"Pan RAS (ON) "	active forms of RAS proteins across wild-type and mutant variants
"PDAC"	pancreatic ductal adenocarcinoma
"RAS"	rat sarcoma, a family of proteins that are critical regulators of cellular signaling pathways; it primarily includes HRAS, KRAS, and NRAS
"SIIP"	switch II pocket (SIIP) is an allosteric drug-binding pocket near the Switch II region of RAS proteins

Cautionary Statement required by Rule 18A.05 of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited: The Company cannot guarantee that it will be able to develop, or ultimately market GFH375, GFS202A and GFH276 successfully. Shareholders and potential investors of the Company are advised to exercise caution when dealing in the shares of the Company.

By order of the Board
GenFleet Therapeutics (Shanghai) Inc.
Dr. Qiang LU
Chairman and Executive Director

Hong Kong, August 20, 2026

As at the date of this announcement, the Board of the Company comprises: (i) Dr. Qiang LU, Dr. Jiong LAN and Ms. ZHANG Wei as executive directors; (ii) Mr. ZHU Jingyang and Ms. TAO Sha as non-executive directors; and (iii) Ms. Christine Shaohua LU-WONG, Dr. ZHOU Demin and Mr. LI Bo as independent

non-executive directors.