AACR 2026: GenFleet Therapeutics Announces Preclinical Data of GFH276, a Molecular Glue Pan RAS (ON) Inhibitor, Demonstrates Lower Preclinical Effective Dose and Synergistic Efficacy with Multiple Standard-of-care Therapies

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GenFleet Therapeutics announced that preclinical data for GFH276, a molecular glue Pan RAS (ON) inhibitor, were presented in a poster session at the 2026 American Association for Cancer Research (AACR) Annual Meeting on April 21 (local time). Preclinical research showed at one-third the dosage of RMC 6236, GFH276 exerted comparable or enhanced tumor growth inhibition (TGI) in multiple RAS-mutant tumor models. Furthermore, GFH276 exhibited robust anti-tumor synergy and extended tumor-free survival when combined with cetuximab, chemotherapy, or anti PD-1 monoclonal antibodies respectively in animal studies. As the world's third Pan RAS inhibitor entering clinical development, early clinical data of GFH276 correlates with its preclinical efficacy and safety profile.

“GenFleet ranks among the world’s leading developers of RAS-focused pipeline, with multiple candidates demonstrating industry leading pace in China or globally. Leveraging an extensive compound library targeting

RAS-inhibiting therapeutics, we have established a suite of continuously upgraded R&D platforms to underpin our forward-looking program initiation. Through the development of small molecule therapies with diverse mechanisms of action, innovative ADCs, and highly differentiated pipeline, we are building a robust and synergistic portfolio, to address unmet clinical needs and deliver transformative treatments for patients with refractory malignancies." stated Fusheng Zhou, Ph.D., Vice President of our GenFleet's Drug Discovery Department.

Preclinical evaluation of GFH276 monotherapy and combination therapy for RAS-mutant tumors (Poster No.: 4565)

Superior TGI achieved at 1/3 dosage of RMC-6236 across multiple tumor models

In models of non-small cell lung cancer (NSCLC), pancreatic cancer, and colorectal cancer (CRC) harboring diverse RAS mutations (including KRAS G12C, G12D, G12V, and G13D), oral administration of GFH276 at 3 mg/kg QD yielded comparable or superior TGI relative to RMC-6236 dosed at 10 mg/kg QD over the same treatment period. In animal models, continuous once-daily oral dosing of GFH276 at 0.3-1 mg/kg for two weeks demonstrated dose-dependent anti-tumor activity.

Broad potential of combination with standard-of-care therapies

In three-week animal studies, low-dose single-agent GFH276 (0.3-1 mg/kg QD) achieved anti-tumor activity comparable to single-agent cetuximab or chemotherapy (gemcitabine plus paclitaxel). Combination of GFH276 with cetuximab (in CRC models) or chemotherapy (in pancreatic ductal adenocarcinoma models) produced marked synergistic activity, with anti-tumor efficacy far exceeding that of either agent alone.In the same three-week studies, single-agent GFH276 (0.3-3 mg/kg QD) outperformed anti-PD-1 antibody monotherapy. Combining GFH276 with anti-PD-1 antibody also yielded strong synergistic anti-tumor effects and significantly improved tumor-free survival for months following treatment cessation, with synergistic activity increasing in a dose-dependent manner.

Activity against diverse RAS mutations and KRAS G12Ci-resistant cell lines

Via a novel CypA-GFH276-RAS complex mechanism, GFH276 inhibits most activated wild-type and mutant RAS isoforms. It demonstrated growth inhibition in multiple KRAS G12C inhibitor-resistant cell lines and potent activity across a broad range of RAS-dependent cancer cell lines, including those harboring RAS alterations, such as RTK alterations (upstream of RAS), and BRAF mutations (downstream of RAS).In prior kinase selectivity

and safety-related profiling, GFH276 showed no off-target activity, supporting its favorable safety and target specificity.GFH276 features a highly differentiated molecular design built around a novel and proprietary macrocyclic core scaffold. This unique structure enables robust global patent position, creating high barriers while endowing the molecule with excellent druggability and promising development potential. It entered a phase I/II clinical trial for RAS-mutant solid tumors in September 2025 and the dose escalation has been conducted in multiple dose levels with a minimum effective dose identified. Preliminary clinical results highlighted favorable pharmacokinetic and tissue-distribution advantages driven by its differentiated molecular structure. Updated clinical data are expected to be presented at global academic conferences later this year.

About RAS and GFH276

RAS proteins, in active GTP-bound or inactive GDP-bound form, are binary molecular switches controlling cellular responses in signaling pathways including RAF-MEK-ERKand PI3K-AKT-mTOR. Three RAS genes encode for protein isoforms, namely Kirsten Ras (KRAS), Harvey Ras (HRAS) and Neuroblastoma Ras (NRAS), and KRAS is the most frequently mutated oncogene in humans.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 press release 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", "predict", "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 GenFleet Therapeutics' 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, GenFleet Therapeutics 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

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