Verastem Oncology Announces Updated Data from Partner GenFleet Therapeutics' Phase 1/2 Monotherapy Study in China of GFH375 (VS-7375) in Advanced KRAS G12D Mutant Pancreatic Ductal Adenocarcinoma

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GFH375 resulted in a 41% ORR for patients with heavily pre-treated pancreatic ductal adenocarcinoma (68% had received 2 or more prior lines of therapy) at the 600 mg daily dose

At month four, the OS rate was 92.2%; median OS has not been reached

91.5% of patients experienced a reduction in tumors and a disease control rate of 96.7%; nearly half the patients evaluated remain on treatment

Low discontinuation rate due to adverse events of 4% demonstrates a manageable safety profile

BOSTON--(BUSINESS WIRE)--Oct. 19, 2025-- Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with RAS/MAPK-pathway-driven cancers, today announced positive, updated efficacy and safety data from partner GenFleet Therapeutics' Phase 1/2 monotherapy study in China of GFH375, an oral KRAS G12D (ON/OFF) inhibitor (VS-7375 outside of China) for patients with KRAS G12D mutant advanced pancreatic ductal adenocarcinoma (PDAC). Among 59 heavily pre-treated patients with advanced disease, who received two or more prior lines of therapy, an overall response rate (ORR) of 41% was achieved at the monotherapy recommended Phase 2 dose (RP2D) of 600 mg daily (QD). The updated data were featured in a late-breaking abstract for oral presentation by GenFleet Therapeutics at the European Society for Medical Oncology (ESMO) Congress 2025 on October 19, 2025, in Berlin, Germany.

"Patients with advanced pancreatic cancer and a KRAS G12D mutation tend to have a worse prognosis compared to other KRAS mutations. We are pleased to see that the updated data presented by our partner, GenFleet Therapeutics, continues to demonstrate encouraging clinical responses at the recommended Phase 2 dose, in a heavily pre-treated, often difficult to treat, patient population," said Dan Paterson, president and chief executive officer of Verastem Oncology. "These data add to the growing body of evidence supporting the therapeutic potential of KRAS G12D inhibition and importantly provide valuable insights as we continue to advance through our Phase 1/2a trial with VS-7375."

ESMO 2025 Presentation Highlights

GenFleet reported that 66 patients with advanced KRAS G12D mutant PDAC were treated with 600 mg QD of GFH375 monotherapy. In the study, 95.5% of patients were diagnosed with stage IV disease at study entry, and 68.2% of patients had received at least two prior lines of anticancer therapies, with 92.4% of patients receiving gemcitabine-based regimens and more than 50% receiving fluorouracil or irinotecan-containing regimens. As of the data cutoff of September 27, 2025, 59 efficacy-evaluable patients had at least one post-treatment tumor assessment and achieved an ORR of 40.7% (24/59) (confirmed and unconfirmed) and a disease control rate (DCR) of 96.7% (57/59) with the majority of patients (91.5%) experiencing a reduction in target lesions. Overall survival (OS) observed at month four was 92.2%. The median OS was not reached as of the data cutoff, with a median follow-up time of 5.65 months. The median progression-free survival (PFS) was 5.52 months with a median follow-up time of 5.65 months and a 4-month PFS rate of 78.2%. At evaluation, 31 (47%) of patients were still on treatment with the longest duration of treatment eclipsing one year (367 days).

The safety profile in PDAC patients was consistent with the previously reported data at recent medical congresses. As of the data cutoff date of August 27, 2025, the most frequent treatment-related adverse events (TRAEs) occurring in ≥20% of patients included diarrhea, neutrophil count decreased, vomiting, nausea, anemia, white blood cell count decreased, decreased appetite, hypoalbuminemia, platelet count decreased, asthenia, aspartate aminotransferase increased, and alanine transferase increased. Grade 3 TRAEs occurred in 20 patients (30.3%) and a Grade 4 TRAE (neutropenia) occurred in one patient (1.5%). Of the 66 patients in the safety population, four patients (6.1%) had a dose reduction and two patients (3%) discontinued due to TRAEs. No TRAE-related deaths were reported. The mean relative dose intensity was 93%.

About KRAS G12D

KRAS G12D represents 26% of all KRAS mutations, making it the most prevalent KRAS mutation in human cancers. The KRAS G12D mutation occurs most commonly in pancreatic (37%), colorectal (12.5%), endometrial (8%), and non-small cell lung (5%) cancers. Currently, no therapies are approved by the U.S. Food and Drug Administration (FDA) specifically targeting KRAS G12D mutations in cancer.

About VS-7375, an Oral KRAS G12D (ON/OFF) Inhibitor

VS-7375 is a potential best-in-class, potent, and selective oral KRAS G12D dual ON/OFF inhibitor. VS-7375 is the lead program from the Verastem Oncology discovery and development collaboration with GenFleet Therapeutics. Verastem announced in April 2025 that the U.S. Investigational New Drug (IND) application for VS-7375 was cleared and initiated a Phase 1/2a clinical trial in June 2025. GenFleet's IND for VS-7375 (known as GFH375 in China) was approved in China in June 2024, and the first patient was dosed in a Phase 1/2 study in July 2024.

About the Phase 1/2a Study of VS-7375

The Phase 1/2a study will be conducted in the U.S., with the potential to expand globally, and will evaluate the safety and efficacy of VS-7375 in

patients with advanced KRAS G12D mutant solid tumors. The starting dose for the Phase 1 study of 400 mg is based on the dose identified in the initial data from the GenFleet study to accelerate the trial's progress. Verastem plans to dose escalate across levels where responses were observed in GenFleet's study and will assess in the Phase 2a portion the efficacy and safety of VS-7375, both as monotherapy and in combination, in patients with advanced solid tumors, such as pancreatic, colorectal, and non-small cell lung cancers.

About the GenFleet Therapeutics Collaboration

The collaboration with GenFleet Therapeutics aims to advance three 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 1 trial. Verastem selected VS-7375 (also known as GFH375), an oral KRAS G12D (ON/OFF) inhibitor, as its lead program in December 2023 and the license for VS-7375 that was exercised in January 2025 is the first one from this collaboration. These licenses give Verastem development and commercialization rights outside the GenFleet markets of mainland China, Hong Kong, Macau, and Taiwan.

About Verastem Oncology

Verastem Oncology (Nasdaq: VSTM) is a biopharmaceutical company committed to developing and commercializing new medicines to improve the lives of patients diagnosed with RAS/MAPK pathway-driven cancers. Verastem markets AVMAPKI™ FAKZYNJA™ CO-PACK in the U.S. Our pipeline is focused on novel small molecule drugs that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth, including RAF/MEK inhibition, FAK inhibition, and KRAS G12D inhibition. For more information, please visit www.verastem.com and follow us on LinkedIn.

Forward-Looking Statements Notice

This press release includes forward-looking statements. These forward-looking statements generally can be identified by the use of words such as "anticipate," "expect," "plan," "could," "may," "believe," "estimate," "forecast," "goal," "project," and other words of similar meaning. Such forward-looking statements address various matters about, among other things, Verastem Oncology's programs and product candidates, strategy, future plans and prospects, including statements related to the potential for and timing of commercialization of product candidates, the expected outcome and benefits of the Company's collaboration with GenFleet Therapeutics (Shanghai), Inc., the timing of commencing and completing trials and compiling data, the expected timing of the presentation of data by the Company and the potential clinical value of various of the Company's clinical trials. Each forward-looking statement contained in this press release is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by any such statement. Applicable risks and uncertainties include, among others: the uncertainties inherent in research and development, such as the possibility of negative or unexpected results of clinical trials; that we may not see a return on investment on the payments we have and may continue to make pursuant to the collaboration and option agreement with GenFleet, or that GenFleet may fail to fully perform under the agreement; that the development and commercialization of our product candidates may take longer or cost more than planned, including as a result of conducting additional studies or our decisions regarding execution of such commercialization; that data may not be available when expected; the risk that our preliminary and interim data may not be representative of more mature data; uncertainties related to the recent change in the U.S. presidential administration, including regulatory and policy changes that may adversely affect our business; risks associated with the current administration's reductions to the FDA's workforce and any subsequent reductions that may lead to disruptions and delays in the FDA's review and oversight of our product candidates and impact the FDA's ability to provide timely feedback on our development programs; that our product candidates may not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients; and the risks identified under the heading "Risk Factors" as detailed in the Company's Annual Report on Form 10-K for the year ended December 31, 2024, as filed with the Securities and Exchange Commission (SEC) on March 20, 2025, as well as the other information we file with the SEC, are possibly realized. We caution investors not to place considerable reliance on the forward-looking statements contained in this press release. You are encouraged to read our filings with the SEC, available at www.sec.gov, for a discussion of these and other risks and uncertainties. The forward-looking statements in this press release speak only as of the date of this press release, and we undertake no obligation to update or revise any of these statements. Our business is subject to substantial risks and uncertainties, including those referenced above. Investors, potential investors, and others should give careful consideration to these risks and uncertainties.

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