Verastem Oncology Announces Encouraging Preliminary Data from Ongoing Phase 1/2a Dose Escalation Trial of VS-7375, an Oral KRAS G12D (ON/OFF) Inhibitor, in Patients with KRAS G12D Mutant Solid Tumors

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First two monotherapy dose levels (400 mg QD and 600 mg QD) cleared, with no dose-limiting toxicities reported

Promising anti-tumor activity observed in patients with various solid tumors, including advanced pancreatic ductal adenocarcinoma

No nausea, vomiting, or diarrhea greater than Grade 1 was observed

Enrollment initiated for VS-7375 in combination with cetuximab in patients with advanced KRAS G12D mutant solid tumors, including colorectal cancer

Plan to report an interim safety and efficacy update on the Phase 1/2a trial in the first half of 2026

BOSTON--(BUSINESS WIRE)--Oct. 23, 2025-- Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with RAS/MAPK-pathway-driven cancers, today announced encouraging preliminary data from the first two dose levels in its ongoing Phase 1/2a clinical trial evaluating VS-7375, a potential best-in-class oral KRAS G12D (ON/OFF) inhibitor, in patients with previously-treated advanced KRAS G12D mutant solid tumors. In addition, while monotherapy dose escalation continues, the Company announced it has initiated patient enrollment for the first dose escalation combination cohort evaluating VS-7375 with cetuximab.

“Preliminary safety and tolerability data from our ongoing Phase 1/2a trial indicate that VS-7375, a potential best-in-class oral KRAS G12D (ON/OFF) inhibitor, can be administered at efficacious doses while effectively managing gastrointestinal side effects,” said Dan Paterson, president and chief executive officer of Verastem Oncology. “While still early, we are pleased to see anti-tumor activity among pre-treated patients with advanced pancreatic cancer and other solid tumors. As we continue monotherapy dose escalation, we are excited to open the combination cohort evaluating VS-7375 with cetuximab just months after trial initiation. By starting this combination cohort at a dose of VS-7375 that has previously demonstrated monotherapy efficacy, we expect to accelerate our clinical development program with other standard-of-care combination cohorts.”

VS-7375-101 is a Phase 1/2a study being conducted in the U.S., with plans underway to expand globally, and is evaluating the safety and efficacy of VS-7375 in patients with previously-treated advanced KRAS G12D mutant solid tumors, including advanced pancreatic ductal adenocarcinoma (PDAC), both as monotherapy and in combination with other standard of care treatments.

In the study, VS-7375 cleared both the 400 mg daily (QD) and 600 mg QD monotherapy doses with no dose-limiting toxicities (DLTs) observed. In addition, no new safety signals have been observed relative to earlier data presentations in both PDAC and non-small cell lung cancer (NSCLC) by our partner, GenFleet Therapeutics, in its ongoing Phase 1 /2 clinical study in China evaluating VS-7375 (known as GFH375). Specifically, at the two dose levels evaluated in the U.S. cohorts, no nausea, vomiting, or diarrhea greater than Grade 1 were reported. Monotherapy dose escalation in the VS-7375-101 study started at the efficacious doses identified in GenFleet’s study, 400 mg QD and 600 mg QD. GenFleet chose 600 mg QD as their recommended Phase 2 dose (RP2D) in China.

Of the five efficacy evaluable patients in the VS-7375-101 study with at least one scan, four out of five patients have had a tumor reduction and are still on treatment. The remaining patients receiving either the 400 mg QD or 600 mg QD doses have not yet reached their first response assessment. The study’s dose escalation continues with evaluating 900 mg QD monotherapy and the combination cohort evaluating VS-7375 with cetuximab is now open and enrolling patients. The cohort will enroll patients with advanced solid tumors, including colorectal cancer.

“We’re encouraged by the early safety experience in this study, including the GI tolerability we’ve seen to date and absence of cutaneous toxicities, along with the early signs of anti-tumor activity. These preliminary findings are promising, and we look forward to the continued evaluation of VS-7375 both as monotherapy and now in combination with cetuximab as there remains a significant unmet need for treatments specifically targeting KRAS G12D-mutant cancers,” said John Hayslip, M.D., chief medical officer of Verastem Oncology.

Subject to the results of the Phase 1 dose escalation combination of VS-7375 and cetuximab, Verastem plans to initiate a combination expansion cohort in colorectal cancer. Following the ongoing monotherapy dose escalation to 900 mg QD, the Company expects to select the recommended Phase 2 dose and advance subsequent efficacy and safety analysis of monotherapy VS-7375 in patient expansion cohorts with advanced PDAC and NSCLC. The Company plans to report an interim safety and efficacy update on the Phase 1/2a trial of VS-7375 in the first half of 2026.

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 (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. Verastem selected VS-7375 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. This license gives Verastem development and commercialization rights outside the GenFleet markets of mainland China, Hong Kong, Macau, and Taiwan.

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

VS-7375-101 is a Phase 1/2a clinical trial being 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 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 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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For Investor and Media Inquiries:
Julissa Viana
Vice President,
Corporate Communications,
Investor Relations & Patient Advocacy
investors@verastem.com or
media@verastem.com

Source: Verastem Oncology