Verastem Oncology Announces First Patient Dosed with VS-7375, an Oral KRAS G12D (ON/OFF) Inhibitor, in a U.S. Phase 1/2a Trial in KRAS G12D Advanced Solid Tumors

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Phase 1 dose-escalation study to evaluate VS-7375 in the U.S., with plans to expand as monotherapy into pancreatic cancer and non-small cell lung cancer cohorts, along with colorectal cancer in combination with cetuximab

BOSTON--(BUSINESS WIRE)--Jun. 24, 2025-- Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with RAS/MAPK pathway-driven cancers, today announced that the first patient has been dosed in VS-7375-101, the U.S. Phase 1/2a clinical trial evaluating VS-7375, a potential best-in-class oral KRAS G12D (ON/OFF) inhibitor, in patients with advanced KRAS G12D mutant solid tumors.

"We continue to make strong progress against our strategic priorities and key milestones that we set at the beginning of the year, including our recent FDA approval and commercial launch and our positive updated results and trial expansion in first-line metastatic pancreatic cancer. We are now excited to have achieved another milestone with the initiation of our first clinical trial and first patient dosed with VS-7375, a potential best-in-class oral KRAS G12D (ON/OFF) inhibitor, in the U.S.," said Dan Paterson, president and chief executive officer of Verastem Oncology.

VS-7375-101 is a Phase 1/2a study being conducted in the U.S., with plans to expand globally, and will evaluate the safety and efficacy of VS-7375 in patients with advanced KRAS G12D mutant solid tumors. The monotherapy dose escalation phase of the study will use a starting dose of 400 mg, based on an efficacious dose identified in the Phase 1/2 study conducted in China by the Company's partner, GenFleet Therapeutics. GenFleet announced encouraging initial safety and efficacy results from its Phase 1 dose-escalation phase of its study of VS-7375 (known as GFH375 in China) at the 2025 ASCO Annual Meeting. Verastem plans to dose-escalate across dose levels where encouraging initial safety and efficacy were observed in patients with advanced KRAS G12D mutant solid tumor cancers in GenFleet's study. Upon successful completion of the dose-escalation phase, the Company will select a recommended Phase 2 dose and assess the efficacy and safety of monotherapy VS-7375 in expansion cohorts of patients with advanced pancreatic cancer and non-small cell lung cancer. In parallel with the monotherapy dose escalation, Verastem will evaluate VS-7375 in combination with cetuximab in advanced solid tumors. 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.

"We are excited that the first patient has initiated treatment with VS-7375 in the U.S. We believe we can leverage VS-7375's dual inhibition of both the ON/OFF states to improve on the efficacy seen to date with other KRAS G12D-selective agents. With the trial underway, we aim to accelerate the program's development given the lack of FDA-approved, KRAS G12D-targeted treatments available to patients with KRAS G12D cancers," said John Hayslip, M.D., chief medical officer of Verastem Oncology. "We are strongly encouraged by the anti-tumor activity seen in the updated Phase 1 data presented at the ASCO Annual Meeting from our partner GenFleet Therapeutics' trial in China. We are advancing VS-7375 in the U.S. to target KRAS G12D mutant advanced solid tumors in areas of significant unmet need, such as pancreatic, colorectal, and lung cancers."

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, development, and commercialization collaboration with GenFleet Therapeutics. Verastem announced in April 2025 that the U.S. Investigational New Drug (IND) application for VS-7375 was cleared, and it initiated a Phase 1/2a clinical trial (NCT07020221), VS-7375-101, in May 2025. GenFleet's IND for VS-7375 (known as GFH375 in China) was approved in China in June 2024, and initial safety and efficacy results from the Phase 1 portion of the study were announced at ASCO 2025. In February 2025, GenFleet announced that the first patient was dosed in the Phase 2 portion of the study.

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; 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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