Verastem Oncology Doses First Patient in TARGET-D 203 Phase 2 Registration-Directed Trial of VS-7375 Oral KRAS G12D (ON/OFF) Inhibitor for KRAS G12D-Mutated Metastatic Colorectal Cancer

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TARGET-D 203 trial to evaluate VS-7375 both as monotherapy and in combination with cetuximab or panitumumab in previously treated metastatic colorectal cancer

A cohort in TARGET-D 203 will also evaluate the combination of VS-7375 with cetuximab and chemotherapy for frontline treatment of metastatic colorectal cancer

KRAS G12D is one of the most common KRAS variants in metastatic colorectal cancer, occurring in approximately 15% of patients

All three TARGET-D registration-directed Phase 2 clinical trials now enrolling following first-patient dosing across pancreatic, colorectal, and lung cancers

BOSTON--(BUSINESS WIRE)--Jul. 28, 2026-- 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 the TARGET-D 203 Phase 2 registration-directed trial evaluating VS-7375, an investigational oral KRAS G12D (ON/OFF) inhibitor with best-in-class potential, to treat patients with KRAS G12D-mutated metastatic colorectal cancer (mCRC). The Company has now initiated treatment across all three of its TARGET-D registration-directed Phase 2 clinical trials evaluating VS-7375 in patients with KRAS G12D-mutated pancreatic, colorectal, and lung cancers.

“KRAS G12D is the most common KRAS mutation found in colorectal cancer and is associated with a worse prognosis for patients compared with KRAS wildtype – underscoring the need for an FDA-approved treatment option specifically for KRAS G12D-mutated cancers. We believe VS-7375 with EGFR blockade has the potential to significantly improve outcomes for patients with KRAS G12D-mutated metastatic colorectal cancer due to its differentiated profile and encouraging preliminary data from our ongoing Phase 1/2 trial,” said Michael Kauffman, M.D., Ph.D., president of development at Verastem Oncology. “VS-7375 has demonstrated preliminary anti-tumor activity in combination with full dose cetuximab with no unexpected toxicities. Dosing the first patient in TARGET-D 203 marks an important milestone in our clinical development program as we continue to advance VS-7375 and build on the encouraging data generated to date.”

TARGET-D 203 (NCT07659795) is a Phase 2, open-label, multi-center study to evaluate VS-7375 at 900 mg once daily (QD) both as monotherapy and in combination with anti-EGFR therapies, including cetuximab or panitumumab, in previously treated KRAS G12D-mutated mCRC. The study is also evaluating VS-7375 in combination with cetuximab and chemotherapy in the first line setting in patients with KRAS G12D-mutated mCRC.

In June 2025, Verastem initiated TARGET-D 101, its Phase 1/2 dose escalation, dose expansion, and combination clinical trial evaluating the safety and efficacy of VS-7375 in patients with KRAS G12D-mutated metastatic pancreatic ductal carcinoma (mPDAC), mCRC, advanced non-small cell lung cancer (NSCLC), and other solid tumor cancers. In a recent update, the Company shared that VS-7375 demonstrated encouraging anti-tumor activity across multiple KRAS G12D-driven tumor types, including mPDAC, mCRC, and advanced NSCLC, with evidence of dose-dependent activity, favorable pharmacokinetics supporting target exposure, and a favorable and manageable safety and tolerability profile. Patient follow-up continues to mature across monotherapy and combination cohorts, and the Company expects to share an update in the second half of 2026.

About Colorectal Cancer
Colorectal cancer (CRC) is the third most common cancer and the second-leading cause of cancer-related death in the U.S. In 2026, an estimated 158,850 people will be diagnosed with colon and rectal cancer. CRC is increasingly affecting younger adults, with one in five new diagnoses now occurring in people younger than age 55, and patients diagnosed before the age of 50 are more likely to present with advanced or metastatic disease at diagnosis. Metastatic colorectal cancer (mCRC), or stage IV disease, occurs when the cancer spreads beyond the colon or rectum to distant organs. Approximately 50% of colorectal cancer cases harbor KRAS mutations, with KRAS G12D accounting for approximately 15% of all CRC cases. Despite advances in the treatment of mCRC, there has been minimal progress in the treatment of patients with KRAS G12D-mutated disease, and no therapies targeting KRAS G12D have been approved for this patient population. Survival outcomes remain poor, underscoring the need for new and improved treatment options.

About KRAS G12D
KRAS G12D represents 26% of all KRAS mutations, making it the most prevalent KRAS mutation in human cancers. When the KRAS gene is mutated, it can promote cancer development and growth. Patients with KRAS G12D-mutant tumors often have poorer outcomes, underscoring the need for therapies designed specifically to inhibit this mutation potently and for a long duration. The KRAS G12D mutation occurs most commonly in pancreatic (40%), colorectal (15%), endometrial (8%), biliary tract (7-15%), 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 & TARGET-D Clinical Program
VS-7375 is a potential best-in-class, potent, and selective investigational oral KRAS G12D dual ON/OFF inhibitor. It is designed to uniquely bind to both the active (ON) and inactive (OFF) states of KRAS G12D, with the potential to inhibit KRAS G12D signaling and tumor growth more completely than compounds that block KRAS G12D only in the OFF state or only in the ON state.

In June 2025, Verastem initiated TARGET-D 101, a Phase 1/2 dose escalation, dose expansion, and combination clinical trial evaluating the safety

and efficacy of VS-7375 in patients with KRAS G12D-mutated metastatic pancreatic ductal carcinoma (mPDAC), metastatic colorectal cancer (mCRC), advanced non-small cell lung cancer (NSCLC), and other solid tumors. Verastem has further expanded the VS-7375 clinical program with the initiation of three Phase 2 registration-directed, open-label clinical trials: TARGET-D 201 (NCT07644559) in second-line advanced or metastatic PDAC, TARGET-D 202 (NCT07659782) in second/third-line advanced or metastatic NSCLC, and TARGET-D 203 (NCT07659795) in metastatic CRC. In June 2026, the company announced the first patient was dosed in the TARGET-D 201 trial, and in July 2026, the first patient was dosed in the TARGET-D 202 trial.

In July 2025, U.S. Food and Drug Administration (FDA) granted Fast Track Designation (FTD) to VS-7375 for the first-line treatment of patients with KRAS G12D-mutated locally advanced or metastatic adenocarcinoma of the pancreas and for the treatment of patients with KRAS G12D-mutated locally advanced or metastatic pancreatic ductal carcinoma who have received at least one prior line of standard systemic therapy. In June 2026, the FDA also granted FTD to VS-7375 for the treatment of adult patients with KRAS G12D-mutated unresectable locally advanced or metastatic non-small cell lung cancer (NSCLC) who have received platinum-based chemotherapy and an anti-PD-(L)1 antibody either concurrently or sequentially.

In December 2023, Verastem selected VS-7375 as its lead program from its collaboration with GenFleet Therapeutics, which 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. In January 2025, Verastem exercised its license for VS-7375. The licenses would give Verastem development and commercialization rights outside the GenFleet markets of mainland China, Hong Kong, Macau, and Taiwan. GenFleet is developing VS-7375 as GFH375 in China.

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

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 anticipated timing for any amendments to the IND application for VS-7375/GFH375, 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 we may not be successful in our continued commercialization of AVMAPKI FAKZYNJA CO-PACK; 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; risks associated with preliminary and interim data, which may not be representative of more mature data; risks associated with the regulatory and policy actions proposed and enacted by the current U.S. presidential administration 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, 2025, as filed with the Securities and Exchange Commission (SEC) on March 4, 2026, 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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