VS-7375 Demonstrates Clinical Activity with a Favorable Safety and Tolerability Profile in TARGET-D 101 Phase 1/2 Clinical Trial in Patients with Advanced KRAS G12D-Mutated Solid Tumors

June 23, 2026 at 4:01 PM EDT

Broad anti-tumor activity observed with VS-7375 across dose levels in multiple solid tumors, including pancreatic, colorectal, and lung cancers

Early evidence of anti-tumor activity with either anti-EGFR therapy or standard-of-care chemotherapy supports broad development strategy including combinations

Favorable safety and tolerability profile characterized by predominately low-grade gastrointestinal adverse events that attenuate after cycle 1; favorable tolerability in combination regimens

Verastem and Erasca announce their intent to evaluate VS-7375 in combination with ERAS-0015, Erasca's investigational pan-RAS molecular glue, in advanced KRAS G12D-mutant solid tumors

Company to host conference call and webcast today at 4:30 p.m. ET

BOSTON--(BUSINESS WIRE)--Jun. 23, 2026-- Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with RAS/MAPK pathway-driven cancers, today announced positive preliminary data from the ongoing TARGET-D 101 Phase 1/2 clinical trial evaluating VS-7375, an investigational oral KRAS G12D (ON/OFF) inhibitor, with best-in-class potential, in patients with advanced KRAS G12D-mutated solid tumors. The data demonstrate encouraging clinical activity along with a favorable safety and tolerability profile across multiple dose levels and tumor types, including metastatic pancreatic ductal carcinoma (mPDAC), metastatic colorectal cancer (mCRC), and advanced non-small cell lung cancer (NSCLC).

"VS-7375 has demonstrated anti-tumor activity across multiple dose levels and tumor types, encouraging signals from rational combination strategies, and a favorable safety profile that improves meaningfully beyond the first treatment cycle, underscoring its potential to be not only the best-in-class oral KRAS G12D inhibitor, but also the preferred treatment option for patients with KRAS-G12D-mutated cancers," said Michael Kauffman, M.D., Ph.D., president of development at Verastem Oncology. "Importantly, VS-7375 has demonstrated compatibility with both anti-EGFR therapy and standard-of-care chemotherapy, supporting the broad development strategy we are pursuing across pancreatic, non-small cell lung, and colorectal cancers. As patient follow-up matures in the TARGET-D 101 study, we are enrolling patients in our three Phase 2 registration-directed studies. We look forward to sharing additional data on VS-7375 in patients with KRAS G12D-mutated cancers later this year."

Highlights of TARGET-D 101 Phase 1/2 Dose Escalation & Dose Expansion Trial
In the TARGET-D 101 trial, dose-escalation is ongoing at 1200 mg once daily (QD). In updated pharmacokinetic (PK) data, the 900 mg QD dose continues to achieve target plasma levels of VS-7375 and provides clear separation from the 600 mg QD dose. VS-7375 demonstrated anti-tumor activity at multiple dose levels, including 400 mg QD, 600 mg QD and 900 mg QD both as monotherapy and in combination with anti-EGFR therapy, across multiple KRAS G12D-driven tumors, including mPDAC, mCRC and advanced NSCLC. In addition, patient follow-up continues to mature across both monotherapy and combination cohorts.

Metastatic PDAC

- Promising clinical activity observed at 900 mg QD monotherapy in previously treated mPDAC, with evidence of dose-dependent anti-tumor activity between 600 mg QD and 900 mg QD
- 93% (13/14) of heavily pretreated (2L-4L) patients with mPDAC receiving 900 mg QD monotherapy achieved greater than 50% reduction in the tumor marker CA19-9. All 14 evaluable patients had elevated baseline CA19-9 levels (>37 U/mL) and at least one scheduled on-treatment CA19-9 assessment. All patients remain on treatment.
- Preliminary data suggest the combination with the anti-EGFR antibody cetuximab is associated with deeper and more rapid tumor reductions, even at a subtherapeutic VS-7375 dose of 400 mg QD.
- Combination cohorts in previously treated mPDAC demonstrate good combinability with standard-of-care chemotherapy, gemcitabine plus Nab-paclitaxel (Gem/NabP). VS-7375 600 mg QD in combination with full-dose Gem/NabP has been DLT-cleared, and enrollment is ongoing with 900 mg QD plus full-dose Gem/NabP.
- Among patients with mPDAC who had received at least one prior therapy (2L+), 7 of 20+ patients enrolled at the 600 mg QD dose level and 1 of 20+ patients enrolled at the 900 mg QD dose level had completed at least six months of follow-up.

Metastatic CRC

- In the mCRC cohort, promising preliminary efficacy was observed with full dose cetuximab at both the 600 mg QD and 900 mg QD dose levels of VS-7375.
- VS-7375 900 mg QD in combination with full dose cetuximab was DLT-cleared in May 2026, with no overlapping toxicities

observed to date. Additional patients will be enrolled at this dose level in the TARGET-D 203 Phase 2 registration-directed mCRC trial.
- Follow-up remains early in the mCRC cohort, with no patients out of 20+ at 600 mg QD in combination with full dose cetuximab having more than six months of follow-up.

Advanced NSCLC

- In the advanced NSCLC cohort, promising preliminary efficacy was observed at 600 mg QD monotherapy.
- Follow-up remains early in the NSCLC cohort, with only one out of 20+ patients at 600 mg QD having more than six months of follow-up.
- The 900 mg QD dose level in advanced NSCLC will be studied in the registration-directed TARGET-D 202 Phase 2 study.

Updated Safety & Tolerability from Phase 1/2 TARGET-D 101
Across monotherapy and combination cohorts in TARGET-D 101, VS-7375 continued to demonstrate a favorable and manageable safety profile, consistent with prior observations and supported by increasing patient exposure and longer follow-up. As of the June 12, 2026 data cutoff, VS-7375 monotherapy has demonstrated a favorable and manageable safety profile at both the 600 mg QD (n=57) and 900 mg QD (n=25) dose levels.

- Treatment-related adverse events (TRAEs) were primarily low-grade nausea, vomiting and diarrhea, which generally diminished over time, with substantially reduced incidence after cycle 1 dosing. The vast majority of the gastrointestinal (GI) side effects were effectively managed with standard supportive care measures, with only 1 reported Grade 3 case of nausea at the 900 mg QD dose that resolved in 4 days after optimization of anti-emetic agents. A very low frequency of rash was observed in either the 600 mg QD or 900 mg QD dose level and no rash above Grade 1.
- TRAEs occurring in more than one patient were largely confined to the first treatment cycle and attenuated substantially thereafter among patients with at least 29 days of follow-up receiving VS-7375 at both the 600 mg QD (n=51) and 900 mg QD (n=22) dose levels.
- No unexpected adverse events (AEs) were observed, and rates of Grade 3 AEs remained low.
- Importantly, no clinically meaningful cytopenias or liver function abnormalities were reported at either the 600 mg QD or 900 mg QD dose level.
- The limited dose-response relationship observed for gastrointestinal AEs is consistent with a localized irritant effect rather than systemic toxicity.
- Emerging longer-term follow-up data are encouraging, with no clinically significant cumulative toxicities observed to date.

VS-7375 Development Collaboration
Verastem and Erasca, Inc., announced today their intent to enter into an agreement to evaluate VS-7375, Verastem's potential best-in-class oral KRAS G12D (ON/OFF) inhibitor, in combination with ERAS-0015, Erasca's potential best-in-class oral pan-RAS molecular glue, across KRAS G12D mutant solid tumor models. Subject to the execution of a definitive agreement and the outcome of the preclinical evaluation, the Companies intend to explore a future clinical trial collaboration to evaluate the combination in patients with advanced solid tumors. Additional details regarding the potential collaboration will be announced at a later date.

"In the first half of this year we have made tremendous progress in advancing the development of VS-7375 in order to bring this truly differentiated KRAS G12D inhibitor with promising emerging clinical efficacy and a favorable safety and tolerability profile both as monotherapy and in combination regimens as quickly as possible to patients," said Dan Paterson, president and chief executive officer of Verastem Oncology. "The momentum behind the VS-7375 program continues to accelerate with the initiation of three Phase 2 registration-directed trials in only three months. We are now expanding the development strategy through a collaboration designed to explore a complementary mechanism and address areas of significant unmet need within KRAS G12D-mutated cancers. Overall, the development strategy for VS-7375 is aimed at maximizing the therapeutic potential of this program across multiple tumor types and treatment settings and supporting multiple potential registration pathways."

Expected Key Milestones:

- Report an update on the TARGET-D 101 trial in 2H 2026.
- Complete target enrollment in TARGET-D 101 PDAC and NSCLC monotherapy cohorts and mCRC cetuximab combination cohorts by the end of June 2026.
- Announce first patient dosed in the TARGET-D 202 and TARGET-D 203 clinical trials in mid-2026.
- Complete enrollment across all three TARGET-D Phase 2 trials by the end of 2026.
- Meet with the U.S. Food and Drug Administration (FDA) before the end of the year to review Phase 3 pivotal trial designs in 1L mPDAC, 1L mCRC and 1L advanced NSCLC.
- Enroll the first patient in each of the Phase 3 pivotal trials in the first half of 2027.

Webcast Information
On June 23rd at 4:30 p.m. ET, a live audio webcast of the call, along with accompanying slides, will be available under "Events & Presentations" in the Investor section of the Company's website, https://investor.verastem.com/events. A replay of the webcast will be archived and available following the event.

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 advanced KRAS G12D mutant 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 pancreatic ductal carcinoma, TARGET-D 202 (NCT07659782) in second/third-line advanced or metastatic non-small cell lung cancer, and TARGET-D 203 (NCT07659795) in metastatic colorectal cancer. On June 16, 2026, the first patient was dosed in the TARGET-D 201 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," "potential," "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; that preclinical studies and any positive preliminary, initial "top-line," and interim data, from our clinical trials of our product candidates may not necessarily be predictive of the results of ongoing or later clinical trials; 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20260623312556/en/

For Investor and Media Inquiries:
Julissa Viana
Senior Vice President, Corporate Communications,
Investor Relations & Patient Advocacy
investors@verastem.com or
media@verastem.com

Source: Verastem Oncology