



Verastem Oncology Announces Positive Updated Results from RAMP 205 Evaluating Avutometinib Plus Defactinib in Combination with Standard-of-Care Chemotherapy in Frontline Metastatic Pancreatic Ductal Adenocarcinoma

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Selected recommended Phase 2 dose: Dose level 1 demonstrated an ORR of 83% (10/12) in frontline metastatic pancreatic ductal adenocarcinoma

Plans for registrational Phase 3 study underway in frontline metastatic pancreatic ductal adenocarcinoma

Company will host an R&D investor webcast on Monday, June 2 at 11:00 am CDT to review the updated RAMP 205 data as well as updated data on VS-7375 presented at ASCO

BOSTON--(BUSINESS WIRE)--May 22, 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 safety and efficacy results from the RAMP 205 Phase 1/2 trial evaluating avutometinib plus defactinib in combination with gemcitabine and Nab-paclitaxel in the front-line for patients with metastatic pancreatic ductal adenocarcinoma (PDAC). As of April 25, 2025, patients in the dose level 1 cohort, which was selected as the recommended Phase 2 dose (RP2D), achieved an overall response rate (ORR) of 83% (10/12).

The Company will host a research and development (R&D) investor webcast on Monday, June 2 at 11:00 am CDT to review the full updated data from RAMP 205 and the updated data from the Phase 1/2 study in China of VS-7375 (also known as GFH375), an oral KRAS G12D (ON/OFF) inhibitor, by partner GenFleet Therapeutics that will be presented in a rapid oral presentation at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL on June 2, 2025.

"The exciting results from the RAMP 205 trial reinforce our commitment to maximizing the synergistic potential of the avutometinib plus defactinib combination in other advanced solid tumors for market expansion opportunities beyond KRAS-mutated recurrent low-grade serous ovarian cancer, for which the combination recently became the first-ever FDA-approved treatment for this disease," said Dan Paterson, president and chief executive officer of Verastem Oncology. "We look forward to the mature data from the Phase 1 portion of the VS-7375 study in China being presented at ASCO and dosing the first patient in our Phase 1/2a trial in the U.S. and in solid tumor cohorts including advanced pancreatic, lung, and colorectal cancers."

Updated Data from RAMP 205 Phase 1/2 Clinical Trial in Frontline Metastatic PDAC

As of April 25, 2025, 60 patients (12 per cohort) had been treated in one of five dose regimens with the combination of avutometinib and defactinib with gemcitabine and Nab-paclitaxel in frontline metastatic PDAC. In the dose level 1 cohort, 12 patients received 2.4 mg of avutometinib twice a week (BIW), 200 mg of defactinib twice a day (BID) for 3 weeks out of every 4 and 800 mg/m² of gemcitabine and 125 mg/m² of Nab-paclitaxel on a schedule of day 1, day 8 and day 15. In dose level 1, 83% (10/12) of patients achieved partial responses (8 confirmed and 2 unconfirmed who remain on treatment). Given these strong and consistent results, the Company has selected dose level 1 as the RP2D, has met the pre-defined criteria to advance beyond the first stage of the expansion study, and is now enrolling up to 29 patients at this dose level.

In evaluating all the dose cohorts, dose level 1 demonstrated the highest response rate and across all five dose cohorts, 92% (48/52) of efficacy evaluable patients showed tumor reduction as best response. Adverse events across all dose cohorts remained generally consistent with the previously announced safety and tolerability profile, and no new safety signals have emerged. While anticipating results from the study expansion cohort, the Company is now developing plans for a registrational Phase 3 front-line metastatic PDAC trial to begin in 2026.

Webcast Information

Verastem will hold an investor webcast on Monday, June 2, at 11:00 am CDT, to review the RAMP 205 updated data and the VS-7375 program including updated data from the study in China. The event will feature members of Verastem's management team and key opinion leaders. A live audio webcast of the call, along with accompanying slides, will be accessible [here](#).

About AVMAPKI and FAKZYNJA Combination Therapy

AVMAPKI (avutometinib) inhibits MEK kinase activity while also blocking the compensatory reactivation of MEK by upstream RAF. RAF and MEK proteins are regulators of the RAS/RAF/MEK/ERK (MAPK) pathway. Blocking RAF and/or MEK activates FAK, a key mediator of drug resistance. FAKZYNJA (defactinib) is a FAK inhibitor and together, the avutometinib and defactinib combination was designed to provide a more complete blockade of the signaling that drives the growth and drug resistance of RAS/MAPK pathway-dependent tumors.

The U.S. Food and Drug Administration (FDA) approved AVMAPKI™ FAKZYNJA™ CO-PACK (avutometinib capsules; defactinib tablets) for the treatment of adult patients with KRAS-mutated recurrent LGSOC who have received prior systemic therapy on May 8, 2025. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. Verastem is also evaluating avutometinib in combination with defactinib and other agents as a potential treatment for patients with advanced pancreatic cancer (RAMP 205; NCT05669482) and advanced KRAS G12C mutant non-small cell lung cancer (RAMP 203; NCT05074810). Avutometinib and defactinib are not approved by the FDA or any other regulatory authority, either in combination or with other therapies, for any of these investigative uses. Neither avutometinib nor defactinib are approved by the FDA or any other regulatory authority on a stand-alone basis for any use.

AVMAPKI FAKZYNJA CO-PACK U.S. Indication

Indication

AVMAPKI FAKZYNJA CO-PACK is indicated for the treatment of adult patients with *KRAS*-mutated recurrent low-grade serous ovarian cancer (LGSOC) who have received prior systemic therapy.

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Important Safety Information

Warnings and Precautions

- **Ocular Toxicities:** Ocular toxicities, including visual impairment and vitreoretinal disorders, occurred. Perform comprehensive ophthalmic evaluation at baseline, prior to cycle 2, every three cycles thereafter, and as clinically indicated. Withhold AVMAPKI FAKZYNJA CO-PACK for ocular toxicities until improvement at the same or reduced dose. Permanently discontinue AVMAPKI FAKZYNJA CO-PACK for any grade 4 toxicity.
- **Serious Skin Toxicities:** Skin toxicities, including photosensitivity and severe cutaneous adverse reactions (SCARs) occurred. Adhere to concomitant medications. Monitor for skin toxicities and interrupt, reduce or permanently discontinue AVMAPKI FAKZYNJA CO-PACK based on severity, tolerability and duration.
- **Hepatotoxicity:** Monitor liver function tests prior to each cycle, on day 15 of the first 4 cycles, and as clinically indicated. Withhold, reduce or discontinue AVMAPKI FAKZYNJA CO-PACK based on severity and persistence of abnormality.
- **Rhabdomyolysis:** Monitor creatine phosphokinase prior to the start of each cycle, on day 15 of the first four cycles, and as clinically indicated. If increased CPK occurs, evaluate patients for rhabdomyolysis or other causes. Withhold, reduce or permanently discontinue AVMAPKI FAKZYNJA CO-PACK based on severity and duration of the adverse reaction.
- **Embryo-Fetal Toxicity:** AVMAPKI FAKZYNJA CO-PACK can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception.

Adverse Reactions

The most common ($\geq 25\%$) adverse reactions, including laboratory abnormalities, were increased creatine phosphokinase, nausea, fatigue, increased aspartate aminotransferase, rash, diarrhea, musculoskeletal pain, edema, decreased hemoglobin, increased alanine aminotransferase, vomiting, increased blood bilirubin, increased triglycerides, decreased lymphocyte count, abdominal pain, dyspepsia, dermatitis acneiform, vitreoretinal disorders, increased alkaline phosphatase, stomatitis, pruritus, visual impairment, decreased platelet count, constipation, dry skin, dyspnea, cough, urinary tract infection, and decreased neutrophil count.

Drug Interactions

- **Strong and moderate CYP3A4 inhibitors:** Avoid concomitant use with AVMAPKI FAKZYNJA CO-PACK.
- **Strong and moderate CYP3A4 inducers:** Avoid concomitant use with AVMAPKI FAKZYNJA CO-PACK.
- **Warfarin:** Avoid concomitant use of AVMAPKI FAKZYNJA CO-PACK with warfarin and use an alternative to warfarin.
- **Gastric acid reducing agents:** Avoid concomitant use of AVMAPKI FAKZYNJA CO-PACK with proton pump inhibitors (PPIs) or H₂ receptor antagonists. If use of an acid-reducing agent cannot be avoided, administer FAKZYNJA 2 hours before or 2 hours after the administration of a locally acting antacid.

Use in Specific Populations

- **Lactation:** Advise not to breastfeed.
- **Fertility:** May impair fertility in males and females.

Click here for full [Prescribing Information](#).

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 plans to initiate a Phase 1/2a clinical trial in mid-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 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 anticipated timing for the initiation of the Phase 1/2a study 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 launch or 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 recent changes in administration policy or actions that may create regulatory uncertainty 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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