



## FDA Approves the AVMAPKI™ FAKZYNJA™ Combination Therapy as the First-Ever Treatment for Adult Patients with KRAS-mutated Recurrent Low-Grade Serous Ovarian Cancer

May 8, 2025 at 1:17 PM EDT

*AVMAPKI plus FAKZYNJA to be commercially available by prescription as a convenient oral combination co-packaged together and will be known as "AVMAPKI FAKZYNJA CO-PACK"*

*Accelerated approval, well ahead of the June 30, 2025 PDUFA action date, was based on the Phase 2 RAMP 201 study that demonstrated a 44% overall response rate in patients with KRAS mutant recurrent LGSOC*

*Verastem to host investor conference call and webcast today at 2:30 pm ET*

BOSTON--(BUSINESS WIRE)--May 8, 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 U.S. Food and Drug Administration (FDA) has approved AVMAPKI™ FAKZYNJA™ CO-PACK (avutometinib capsules; defactinib tablets) for the treatment of adult patients with KRAS-mutated recurrent low-grade serous ovarian cancer (LGSOC) who received prior systemic therapy. AVMAPKI FAKZYNJA CO-PACK is the first and only FDA-approved medicine for this disease. This indication is approved under accelerated approval based on the 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. AVMAPKI plus FAKZYNJA is only commercially available in the U.S. as an oral combination co-pack with the two prescription products, known as "AVMAPKI FAKZYNJA CO-PACK."

This press release features multimedia. View the full release here: <https://www.businesswire.com/news/home/20250508131607/en/>



"Today's approval of AVMAPKI FAKZYNJA CO-PACK for patients with KRAS-mutated recurrent low-grade serous ovarian cancer represents not only the first-ever FDA-approved treatment specifically for this rare cancer but also a new day for people living with this disease who have been in desperate need of new treatment options," said Dan Paterson, president and chief executive officer of Verastem Oncology. "We are very proud to bring two innovative medicines in one combination treatment to the LGSOC community. We thank the researchers, patients, and their families participating in our clinical trials, the patient advocacy community, the FDA, and everyone at Verastem for their dedication and commitment to helping us bring AVMAPKI FAKZYNJA CO-PACK to patients in the U.S."

The accelerated approval of AVMAPKI FAKZYNJA CO-PACK is based on the Phase 2 RAMP 201 clinical trial, which evaluated the combination of AVMAPKI and FAKZYNJA in adult patients with measurable KRAS-mutated recurrent LGSOC.

"Low-grade serous ovarian cancer is a rare and highly recurrent cancer with limited effective treatment options. This first-ever FDA approval in this disease was based on the primary analysis of the Phase 2 RAMP 201 trial, in which the combination of avutometinib and defactinib resulted in a significant overall response rate for

Product shot.

patients with a KRAS mutation while being generally well tolerated," said Rachel Grisham, M.D., Section Head, Ovarian Cancer at Memorial Sloan Kettering Cancer Center in New York, NY and Global Lead Principal Investigator of GOG-3097/ENGOT-ov81/GTG-UK/RAMP 301. "The approval of avutometinib plus defactinib brings a much-needed therapeutic option to patients and establishes this combination as the new standard of care for women with recurrent low-grade serous ovarian cancer harboring a KRAS mutation. I look forward to progressing the confirmatory Phase 3 trial, RAMP 301, where we look to continue to support the ongoing body of research of this combination in women with and without a KRAS mutation."

"To see our early research in both the FRAME and RAMP 201 trial in recurrent low-grade serous ovarian cancer advance the combination of avutometinib and defactinib to now be the first-ever FDA-approved therapy for this disease is what gives us real hope when treating patients with rare or difficult-to-treat gynecological cancers," said Professor Susana Banerjee, M.B.B.S., M.A., Ph.D., F.R.C.P, Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust and Team Leader in Women's Cancers at The Institute of Cancer Research, London and Global Lead Principal Investigator of ENGOTov60/GOG3052 /NCRI/RAMP201. "With this approval, we thank all of the patients and researchers who participated in this trial, and the low-grade serous ovarian cancer community for their contributions to help bring the first FDA-approved treatment for KRAS-mutated recurrent LSGOC and changing the treatment possibilities for RAS/MAPK-pathway-driven cancers. We now need to build on this milestone to bring this new treatment to patients around the world."

Prior to this approval, there were no FDA-approved treatments specifically for KRAS-mutated recurrent LGSOC, a rare and distinct ovarian cancer that differs from high-grade serous ovarian cancer in both its biology and how it responds to treatment.

"One of the most devastating aspects of my LGSOC diagnosis was learning there are no FDA-approved treatments for this rare cancer. While there were some treatment options at the time that I could try, I made it my mission to advocate for research specific to my disease," said Nicole Andrews, chair of the STAAR Low-Grade Serous Ovarian Cancer Foundation. "Today we're celebrating a milestone with the first-ever FDA-approved treatment option specifically for patients with recurrent LGSOC with a KRAS mutation. The low-grade serous ovarian cancer community is hopeful and excited about the potential benefits of this treatment and the progress toward improving the diagnosis, awareness, and research for LGSOC."

AVMAPKI FAKZYNJA CO-PACK is the first treatment to receive regulatory approval anywhere in the world, specifically for KRAS-mutated recurrent LGSOC. The Company believes AVMAPKI FAKZYNJA CO-PACK is also the first-ever oral, novel/novel combination therapy approved in oncology. Verastem initiated a rolling new drug application (NDA) with the FDA in May 2024 and completed its NDA submission in October 2024. The FDA granted Priority Review, and the approval was received in advance of its Prescription Drug User Fee Act (PDUFA) action date of June 30, 2025. The FDA granted Breakthrough Therapy Designation for the treatment of patients with recurrent LGSOC after one or more prior lines of therapy, including platinum-based chemotherapy, in May 2021. Avutometinib alone or in combination with defactinib was also granted Orphan Drug Designation by the FDA for the treatment of LGSOC.

The AVMAPKI FAKZYNJA CO-PACK is expected to be available for adult patients with KRAS-mutated recurrent LGSOC in the U.S. in one week.

### **Verastem's Commitment to Patient Support**

Verastem Oncology is committed to providing patient access and reimbursement support through its Verastem Cares™ program in the U.S. Verastem Cares™ offers a range of patient access and reimbursement support services to help U.S. patients prescribed AVMAPKI FAKZYNJA CO-PACK receive treatment access. Verastem Cares™ case managers can be reached at 1-866-351-8372 between 8:00 am-8:00 pm Eastern Time, Monday through Friday.

### **Verastem to Host Investor Call on AVMAPKI FAKZYNJA CO-PACK FDA Approval**

Verastem will hold an investor conference call and webcast today at 2:30 pm ET, to discuss the FDA approval of AVMAPKI FAKZYNJA CO-PACK. To access the conference call, please dial (844) 763-8274 (local) or (412) 717-9224 (international) at least 10 minutes prior to the start time and ask to be joined into the Verastem Oncology conference call. A live audio webcast of the call, along with accompanying slides, will be accessible under "Events & Presentations" in the Investors & Media section of the Company's website at [www.verastem.com](http://www.verastem.com).

### **Basis of Approval: RAMP 201 Trial Results**

The efficacy of AVMAPKI and FAKZYNJA, in combination, was evaluated in the RAMP 201 clinical trial (NCT04625270), an open-label, multicenter study that included 57 adult patients with measurable KRAS-mutated recurrent LGSOC. Patients were required to have received at least one prior systemic therapy, including a platinum-based drug. Patients received AVMAPKI 3.2 mg orally twice weekly for the first three weeks out of a four-week cycle and FAKZYNJA 200 mg orally twice daily for the first three weeks out of a four-week cycle until disease progression or unacceptable toxicity. The major efficacy outcome measure was overall response rate (ORR) assessed by blinded independent review committee (BIRC) according to Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1. An additional efficacy outcome measure was duration of response (DOR). Tumor response assessments occurred every eight weeks for the first 72 weeks and every 12 weeks thereafter.

In the study, AVMAPKI and FAKZYNJA, in combination, showed in patients with a KRAS mutation a confirmed ORR by BICR of 44% (25/57; 95% CI: 31-58). The median DOR ranged from 3.3 to 31.1 months in the KRAS mutant population.

The safety of AVMAPKI and FAKZYNJA, in combination, was evaluated in 57 patients with KRAS-mutated recurrent LGSOC. Possible serious side effects with AVMAPKI FAKZYNJA CO-PACK include ocular disorders, skin toxicities (rash), hepatotoxicity, rhabdomyolysis, and fetal harm when administered during pregnancy. The most common side effects, including laboratory changes, of AVMAPKI FAKZYNJA CO-PACK include increased levels of an enzyme in the blood (CPK), nausea, fatigue, abnormal liver test (AST), and rash.

### **About Low-Grade Serous Ovarian Cancer (LGSOC)**

LGSOC is a rare ovarian cancer that is insidious and persistent. LGSOC is distinct and different from high-grade serous ovarian cancer (HGSOC) and requires different treatment. LGSOC is highly recurrent and less sensitive to chemotherapy compared to HGSOC. Approximately 6,000-8,000 women in the U.S. and 80,000 worldwide are living with this disease. LGSOC affects younger women with bimodal peaks of diagnosis at ages between 20-30 and 50-60 and has a median survival of approximately ten years. Approximately 70 percent of LGSOC shows RAS pathway-associated mutations, and 30 percent of people with LGSOC have a KRAS mutation. The majority of patients report a negative impact of LGSOC on their mental and physical health, fertility, and long-term quality of life. The current standard of care for LGSOC includes hormone therapy and chemotherapy.

### **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.

*Additional clinical investigations:* Verastem Oncology is conducting clinical trials with avutometinib with and without defactinib in RAS/MAPK-driven tumors as part of its Raf And Mek Program or RAMP. RAMP 301 (GOG-3097/ENGOT-ov81/GTG-UK) (NCT06072781), is an international Phase 3 confirmatory trial evaluating the combination of avutometinib and defactinib versus standard chemotherapy or hormonal therapy for the treatment of recurrent low-grade serous ovarian cancer (LGSOC) with and without a KRAS mutation. RAMP 203 (NCT05074810) is a Phase 1/2, multicenter, open-label, dose evaluation/expansion study, being conducted in collaboration with Amgen, evaluating the efficacy and safety of avutometinib and sotorasib with or without defactinib in patients with KRAS G12C mutant non-small cell lung cancer (NSCLC) who have not been previously treated with a KRAS G12C inhibitor as well as in patients who have been previously treated with a KRAS G12C inhibitor (NCT05074810). RAMP 205 (NCT05669482), a Phase 1b/2 clinical trial evaluating avutometinib and defactinib with gemcitabine/nab-paclitaxel in patients with front-line metastatic pancreatic cancer, is supported by the PanCAN Therapeutic Accelerator Award. 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.

Additional media assets are available on Verastem Oncology's [website](#).

## **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 Disorders:** 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 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](http://www.verastem.com) and follow us on [LinkedIn](#).

### Forward-Looking Statement

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. All statements other than historical statements of fact regarding Verastem's expectations, beliefs, goals, plans or prospects including, without limitation, statements about AVMAPKI FAKZYNJA CO-PACK's potential to benefit adult patients living with KRAS-mutated recurrent low-grade serous ovarian cancer in the United States, AVMAPKI FAKZYNJA CO-PACK's potential to be a transformational medicine, and AVMAPKI FAKZYNJA CO-PACK's potential to be an important treatment option for patients with KRAS-mutated recurrent low-grade serous ovarian cancer should be considered forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "would," "could," "should," "continue," "can," "promising" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement.

Actual results and future plans may differ materially from those indicated by these forward-looking statements as a result of various important risks, uncertainties and other factors, including, without limitation, risks and uncertainties relating to: the launch AVMAPKI FAKZYNJA CO-PACK in the United States including having the product available in the market following launch and thereafter; the adoption of the product by health care professionals; establishing favorable pricing for the product and securing reimbursement coverage from third-party payors, including government agencies, for the product; establishing the product as the standard of care for KRAS-mutant recurrent LGSOC; actions or advice of regulatory agencies and our ability to obtain and maintain regulatory approval for our product; the market opportunities for AVMAPKI FAKZYNJA CO-PACK are based on internal and third-party estimates that may prove to be incorrect; that there may be competitive developments affecting our product candidates; that data may not be available when expected; that our product may cause adverse safety events or unexpected concerns may arise from additional data or analysis, or result in unmanageable safety profiles as compared to its level of efficacy; that we may be unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our product that require or would commercially benefit from such tests, or experience significant delays in doing so; that our product may experience manufacturing or supply interruptions or failures; that we face substantial competition, which may result in others developing or commercializing products before or more successfully than we do which could result in reduced market share or market potential for our product candidates; the discovery and development of novel drug candidates and delivery approaches and successful demonstration of the efficacy and safety of our product candidates; the pre-clinical and clinical results for our product candidates; that we may not have sufficient cash to fund our contemplated operations, including certain of our product commercialization and development programs; that we may not attract and retain high quality personnel; that we may not be able to expand the approved indication for AVMAPKI FAKZYNJA CO-PACK; that we may not be able to successfully launch, market and sell AVMAPKI FAKZYNJA CO-PACK in the United States and realize all or a substantial portion of the potential market opportunity; that we may not be able to successfully launch, market and sell approved products globally; that there may be delays, interruptions or failures in the manufacture and supply of our product candidates or marketed products; that we successfully obtain, maintain and protect intellectual property on our development and marketed products; that we are able to manage growth and operating expenses through disciplined investment in operations and able to achieve a self-sustainable financial profile in the future and avoid or successfully manage unexpected expenditures; that we are able to maintain strategic business collaborations; the dependence on third parties for the development and commercialization of certain products; the risk of future government investigations and substantial changes in governmental policies, regulations, funding and enforcement; as well as those risks and uncertainties more fully discussed in the "Risk Factors" filed with Verastem's 2024 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on March 20<sup>th</sup>, 2025, as may be updated from time to time in Verastem's subsequent Quarterly Reports on Form 10-Q, and in other filings that Verastem makes with the SEC.

Dr. Grisham has financial interests related to Verastem Oncology.

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