Verastem Oncology Provides Update on RAMP 203 Phase 1/2 Clinical Trial for Advanced KRAS G12C Mutant Non-Small Cell Lung Cancer

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BOSTON--(BUSINESS WIRE)--Dec. 29, 2025-- Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with RAS/MAPK pathway-driven cancers, today announced that following evaluation of interim data from the RAMP 203 clinical trial in advanced KRAS G12C-mutated non-small cell lung cancer (NSCLC) it will discontinue the trial to focus resources on clinical development of VS-7375, an oral KRAS G12D (ON/OFF) inhibitor, in advanced NSCLC and other solid tumors. There will be no further enrollment and patients currently enrolled will have the option to continue treatment per investigator discretion. This decision reflects the evolving treatment landscape for KRAS G12C inhibitors and the strategic prioritization of programs with the greatest potential impact for patients living with advanced lung cancer.

“RAMP 203 has provided important insights into treatment strategies and demonstrated proof-of-concept. While avutometinib plus defactinib combined well with a G12C inhibitor to drive early and sustained anti-tumor responses, next generation G12C inhibitors are establishing a new benchmark with higher response rates. Accordingly, we are prioritizing our clinical development of VS-7375, a potentially best-in-class oral KRAS G12D (ON/OFF) inhibitor, that demonstrated a 69% response rate (11 of 16, both confirmed and unconfirmed) in advanced KRAS G12D NSCLC and has the potential to help more patients with its differentiated approach in multiple solid tumors; and the RAMP 205 clinical trial evaluating avutometinib plus defactinib in combination with chemotherapy in first line metastatic pancreatic cancer,” said John Hayslip, chief medical officer at Verastem Oncology. “We sincerely appreciate and thank the investigators, patients, and families who participated in this program as these clinical outcomes will contribute to the development of novel therapies urgently needed for this challenging cancer.”

RAMP 203 is a Phase 1/2 clinical trial being conducted in collaboration with Amgen evaluating avutometinib, an oral RAF/MEK clamp, and *LUMAKRAS*™(sotorasib) in a “doublet combination” and also with defactinib, an oral FAK inhibitor, as a “triplet combination” in patients naïve to or previously treated with a KRAS G12C inhibitor.

As of November 26, 2025, the data cutoff, 66 patients were treated at the recommended Phase 2 dose (RP2D), had at least one tumor scan, and were evaluable for efficacy.

- For the doublet combination, 30 G12C-inhibitor treatment-naïve patients were efficacy evaluable and achieved an overall response rate (ORR) of 40% (12/30) and the median progression-free survival (mPFS) was 11.1 months with a median follow up of 15.9 months.
- In the previously G12C-inhibitor treated group for the doublet combination, 21 patients were efficacy evaluable and achieved an ORR of 9.5% (2/21) and a mPFS of 3.7 months with a median follow up time of 10.8 months.
- Among six G12C-inhibitor treatment-naïve patients in the triple combination, four were evaluable for efficacy and achieved an ORR of 50% (2/4); one confirmed and one unconfirmed, and one additional patient had a best response of stable disease (SD).
- Among 12 patients on the triplet combination who were previously treated with a KRAS G12C inhibitor, 11 were efficacy evaluable and four (36%) showed greater than 30% tumor reduction with seven still ongoing as of the data cutoff.
- Median PFS could not be determined in the triplet treatment-naïve combination cohort, whereas those previously treated with a G12C inhibitor in the triplet combination showed a median PFS of 3.6 months.
- Across the doublet and triplet combinations evaluated, no dose-limiting toxicities were observed. Treatment related adverse events were generally manageable, with nausea (56.8%), diarrhea (52.7%), and fatigue (45.9%) the most common.

The Company is assessing opportunities to share the data in the future.

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 conducting RAMP 301 (GOG-3097/ENGOT-ov81/GTG-UK) (NCT06072781), 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. Verastem is also evaluating avutometinib plus defactinib with standard-of-care chemotherapy as a potential treatment in the first line for patients with advanced pancreatic cancer (RAMP 205; NCT05669482). 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 (SCARSs) 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 (≥ 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 and follow us on LinkedIn.

Forward-looking statements:

Certain of the statements made in this press release, including those relating to Verastem Oncology's clinical development programs, are 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. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include, without limitation: our ability to successfully complete clinical development programs and any subsequent commercialization of the assets being developed; As a result of these and other factors, we may not achieve the plans, intentions or expectations disclosed in our forward-looking

statements, and you should not place undue reliance on these forward-looking statements, which apply only as of the date of this press release. Other risks and uncertainties, including those 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, may possibly be 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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