



## **Verastem Oncology Completes Rolling NDA Submission to the FDA for Avutometinib Plus Defactinib as a Treatment for Recurrent KRAS Mutant Low-Grade Serous Ovarian Cancer**

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*Recurrent low-grade serous ovarian cancer is a rare cancer with no FDA-approved treatments*

*Company seeking accelerated approval and priority review of its NDA submission in patients with KRAS mutant low-grade serous ovarian cancer; FDA filing decision expected before the end of 2024 with potential for FDA approval decision by mid-2025*

BOSTON--(BUSINESS WIRE)--Oct. 31, 2024-- Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with cancer, today announced that the Company has completed its rolling New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for the investigational and potential first-in-class combination of avutometinib, an oral RAF/MEK clamp, and defactinib, an oral selective FAK inhibitor, for adults with recurrent KRAS mutant low-grade serous ovarian cancer (LGSOC), who received at least one prior systemic therapy.

There are currently no FDA-approved treatments specifically for LGSOC, a rare and distinct ovarian cancer that differs from high-grade serous ovarian cancer in both its biology and behavior. Verastem submitted the NDA under the FDA's Accelerated Approval pathway and requested a Priority Review based on the combination's potential to address significant unmet medical need among patients with recurrent LGSOC. If granted, the FDA review will be completed within six months following the 60-day filing period. If approved, Verastem expects that avutometinib plus defactinib will be the first-ever FDA-approved treatment specifically for adult patients in the United States with recurrent KRAS mutant LGSOC.

"We believe that avutometinib in combination with defactinib has the potential to change the treatment paradigm for patients with recurrent KRAS mutant low-grade serous ovarian cancer," said Dan Paterson, president and chief executive officer of Verastem Oncology. "Completing our NDA submission is a significant milestone not only for Verastem as we plan for potential FDA approval in mid-2025, but also for patients as there are no FDA-approved treatments specifically for this rare ovarian cancer."

The Company initiated the rolling NDA submission in May 2024 after reviewing preliminary data with the FDA. Updated results from the Phase 2 registration-directed RAMP 201 study were presented in a late-breaking oral plenary presentation at the International Gynecologic Cancer Society 2024 Annual Meeting and demonstrated in patients with KRAS mutant LGSOC, a confirmed overall response rate (ORR) of 44%, a median progression free survival (PFS) of 22 months, and a disease control rate at 6 months of 70%. The updated data continue to demonstrate avutometinib in combination with defactinib is generally well-tolerated, with a 10% discontinuation rate due to adverse events (AEs) across all patients (both KRAS mutant and KRAS wild-type). The NDA submission also includes supportive data from the FRAME Phase 1 trial, the first study conducted with the combination in recurrent LGSOC.

The FDA previously granted Breakthrough Therapy Designation for avutometinib plus defactinib for the treatment of patients with recurrent LGSOC after one or more prior lines of therapy, including platinum-based chemotherapy. Avutometinib alone or in combination with defactinib was also granted Orphan Drug Designation by the FDA for the treatment of LGSOC.

The Company is currently enrolling patients with recurrent LGSOC regardless of KRAS mutation status for RAMP 301, an international Phase 3 trial, which will serve as a confirmatory study for the initial indication and has potential to support an expanded indication regardless of KRAS mutation status.

### **About RAMP 201**

RAMP 201 (ENGOTov60/GOG3052) is an adaptive, two-part multicenter, parallel cohort, randomized, open-label trial to evaluate the efficacy and safety of avutometinib alone and in combination with defactinib in patients with recurrent low-grade serous ovarian cancer. The first part of the study (Part A) determined the selection of the go forward regimen, which was the combination of avutometinib and defactinib versus avutometinib alone, based on overall response rates. The expansion phases of the trial (Parts B and C) are evaluating the safety and efficacy of the go forward regimen of avutometinib 3.2 mg twice weekly and defactinib 200 mg twice daily. The Part D portion of the trial is evaluating a low dose of avutometinib in combination with defactinib to inform individualized dose reduction.

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

LGSOC is a rare ovarian cancer that is insidious, persistent and ultimately fatal. 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. 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 this disease includes hormone therapy and chemotherapy, but there are no treatments specifically approved by the U.S. Food and Drug Administration to treat LGSOC.

### **About the Avutometinib and Defactinib Combination**

Avutometinib is a RAF/MEK clamp that induces inactive complexes of MEK with ARAF, BRAF and CRAF potentially creating a more complete and durable anti-tumor response through maximal RAS/MAPK pathway inhibition. In contrast to currently available MEK-only inhibitors, avutometinib

blocks both MEK kinase activity and the ability of RAF to phosphorylate MEK. This unique mechanism allows avutometinib to block MEK signaling without the compensatory activation of MEK that appears to limit the efficacy of other MEK-only inhibitors.

Verastem Oncology is currently conducting clinical trials with avutometinib in RAS/MAPK driven tumors as part of its **Raf And Mek Program** or RAMP. Verastem is currently enrolling patients and activating sites for RAMP 301 (NCT06072781) an international Phase 3 confirmatory trial evaluating the combination of avutometinib and defactinib, a selective FAK inhibitor, versus standard chemotherapy or hormonal therapy for the treatment of recurrent low-grade serous ovarian cancer (LGSOC). RAMP 201 (NCT04625270) is a Phase 2 registration-directed trial of avutometinib in combination with defactinib in patients with recurrent LGSOC and enrollment has been completed for the RAMP 201 trial.

Verastem completed its rolling New Drug Application (NDA) submission to the U.S. Food and Drug Administration (FDA) for the investigational combination of avutometinib and defactinib in adults with recurrent KRAS mutant LGSOC who received at least one prior systemic therapy in October 2024, with a potential FDA decision mid-2025. The FDA granted Breakthrough Therapy Designation of the investigational combination of avutometinib and defactinib for the treatment of patients with recurrent LGSOC after one or more prior lines of therapy, including platinum-based chemotherapy. Avutometinib alone or in combination with defactinib was also granted Orphan Drug Designation by the FDA for the treatment of LGSOC.

Verastem Oncology has established clinical collaborations with Amgen and Mirati to evaluate LUMAKRAS™ (sotorasib) in combination with avutometinib and defactinib and KRAZATI™ (adagrasib) in combination with avutometinib in KRAS G12C mutant NSCLC as part of the RAMP 203 (NCT05074810) and RAMP 204 (NCT05375994) trials, respectively. The 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. FDA granted Orphan Drug Designation to avutometinib and defactinib combination for the treatment of pancreatic cancer.

### **About Verastem Oncology**

Verastem Oncology (Nasdaq: VSTM) is a late-stage development biopharmaceutical company committed to the development and commercialization of new medicines to improve the lives of patients diagnosed with cancer. Our pipeline is focused on RAS/MAPK-driven cancers, specifically novel small molecule drugs that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth, including RAF/MEK inhibition and FAK inhibition. For more information, please visit [www.verastem.com](http://www.verastem.com) and follow us on [LinkedIn](#).

### **Forward-Looking Statements**

This press release includes forward-looking statements about, among other things, Verastem Oncology's programs and product candidates, strategy, future plans and prospects, including statements related to the expected timing for the FDA review of the NDA submission for the avutometinib and defactinib combination in LGSOC, the ongoing discussions with the FDA and the ability to obtain Accelerated Approval and Priority Review of the mature RAMP 201 data, the potential of the combination of avutometinib and defactinib to change the way patients with recurrent LGSOC are treated, the potential of the results of the RAMP 301 Phase 3 trial to expand the indication regardless of KRAS mutation status, the structure of our planned and pending clinical trials, the potential clinical value of various of the Company's clinical trials, including the RAMP 201, RAMP 205 and RAMP 301 trials, interactions with regulators, the timeline and indications for clinical development, regulatory submissions and the potential for and timing of commercialization of product candidates. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "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 our actual results to differ materially from those expressed or implied in the forward-looking statements we make. Applicable risks and uncertainties include the risks and uncertainties, among other things, regarding: the success in the development and potential commercialization of our product candidates, including avutometinib in combination with other compounds, including defactinib, LUMAKRAS™ and others; the uncertainties inherent in research and development, such as negative or unexpected results of clinical trials, the occurrence or timing of applications for our product candidates that may be filed with regulatory authorities in any jurisdictions; whether and when regulatory authorities in any jurisdictions may approve any such applications that may be filed for our product candidates, and, if approved, whether our product candidates will be commercially successful in such jurisdictions; our ability to obtain, maintain and enforce patent and other intellectual property protection for our product candidates; the scope, timing, and outcome of any legal proceedings; decisions by regulatory authorities regarding trial design, labeling and other matters that could affect the timing, availability or commercial potential of our product candidates; whether preclinical testing of our product candidates and preliminary or interim data from clinical trials will be predictive of the results or success of ongoing or later clinical trials; that the timing, scope and rate of reimbursement for our product candidates is uncertain; that the market opportunities of our drug candidates are based on internal and third-party estimates which may prove to be incorrect; that third-party payors (including government agencies) may not reimburse; that there may be competitive developments affecting our product candidates; that data may not be available when expected; that enrollment of clinical trials may take longer than expected, which may delay our development programs, including delays in review by the FDA of our NDA submission in recurrent KRAS mutant LGSOC if enrollment in our confirmatory trial is not well underway at the time of submission, or that the FDA may require the Company to enroll additional patients in the Company's ongoing RAMP-301 confirmatory Phase 3 clinical trial prior to FDA taking action on our NDA seeking accelerated approval; risks associated with preliminary and interim data, which may not be representative of more mature data, including with respect to interim duration of therapy data; that our product candidates will cause adverse safety events and/or unexpected concerns may arise from additional data or analysis, or result in unmanageable safety profiles as compared to their levels of efficacy; that we may be unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our product candidates that require or would commercially benefit from such tests, or experience significant delays in doing so; that the mature RAMP 201 data and associated discussions with the FDA may not support the scope of our NDA submission for the avutometinib and defactinib combination in LGSOC, including with respect to KRAS wild type LGSOC; that our product candidates may experience manufacturing or supply interruptions or failures; that any of our third party contract research organizations, contract manufacturing organizations, clinical sites, or contractors, among others, who we rely on fail to fully perform; 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; that we will be unable to successfully initiate or complete the clinical development and eventual commercialization of our product candidates; that the development and commercialization of our product candidates will take longer or cost more than planned, including as a result of conducting additional studies or our decisions regarding execution of such commercialization; that we may not have sufficient cash to fund our contemplated operations, including certain of our product development programs; that we may not attract and retain high quality personnel; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the avutometinib license agreement; that the total addressable and target markets for our product candidates might be smaller than we are presently estimating; that we or Secura Bio, Inc. (Secura) will fail to fully perform under the asset

purchase agreement with Secura, including in relation to milestone payments; that we will 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 Therapeutics (Shanghai), Inc. (GenFleet), or that GenFleet will fail to fully perform under the agreement; that we may not be able to establish new or expand on existing collaborations or partnerships, including with respect to in-licensing of our product candidates, on favorable terms, or at all; that we may be unable to obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that we will not pursue or submit regulatory filings for our product candidates; and that our product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients.

Other risks and uncertainties include those identified under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2023 as filed with the Securities and Exchange Commission (SEC) on March 14, 2024 and in any subsequent filings with the SEC, which are available at [www.sec.gov](http://www.sec.gov). The forward-looking statements contained in this press release reflect Verastem Oncology's views as of the date hereof, and the Company does not assume and specifically disclaims any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by law.

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