Verastem Oncology Outlines 2025 Strategic Priorities and Milestones for Novel Pipeline Targeting RAS/MAPK Pathway-Driven Cancers

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Avutometinib plus defactinib granted priority review by FDA, under the accelerated approval pathway, for recurrent KRAS mutant LGSOC; PDUFA action date set for June 30, 2025

Potential U.S. commercial launch in recurrent KRAS mutant LGSOC planned for mid-2025

RAMP 205 trial in 1L metastatic pancreatic cancer continues to progress, with updated data expected in Q1 2025 to guide RP2D decision for trial expansion

VS-7375 is on track for U.S. IND filing in Q1 2025 with plans for a Phase 1/2a study in mid-2025

Cash position following recent debt and equity financing provides expected runway beyond potential FDA approval and helps to advance early-stage pipeline

BOSTON--(BUSINESS WIRE)--Jan. 23, 2025-- Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with RAS/MAPK pathway-driven cancers, today announced its 2025 priorities and upcoming catalysts for its novel clinical pipeline.

"We ended 2024 having made tremendous progress across our pipeline programs, including FDA acceptance of our NDA with Priority Review for avutometinib plus defactinib in recurrent KRAS mutant low-grade serous ovarian cancer. As we head into 2025, we are building on the foundational milestones achieved in 2024 and are poised for a transformative year of growth as we evolve into a commercial-stage company while advancing several clinical programs," said Dan Paterson, president and chief executive officer at Verastem Oncology. "With the addition of VS-7375, a potential best-in-class oral KRAS G12D (ON/OFF) inhibitor, we are well-positioned to further establish our leadership in targeting RAS/MAPK pathway-driven cancers, including metastatic pancreatic cancer, non-small cell lung cancer, and KRAS G12D mutant solid tumors."

In 2025, Verastem will focus on three strategic priorities to drive sustainable long-term growth:

- Successfully launch avutometinib plus defactinib in recurrent KRAS mutant low-grade serous ovarian cancer (LGSOC) in the U.S. and continue to advance the regulatory pathway in Japan and Europe
- Maximize the synergistic potential of the avutometinib plus defactinib combination in other advanced solid tumors for market expansion opportunities
- Advance its novel, early-stage pipeline, including its potential best-in-class oral KRAS G12D (ON/OFF) inhibitor, to create multiple opportunities to demonstrate transformative outcomes for people living with RAS/MAPK pathway-driven cancers

Successfully Launch Avutometinib Plus Defactinib in the U.S. and Continue to Advance the Regulatory Pathway in Japan and Europe

On December 30, 2024, the U.S. Food and Drug Administration (FDA) accepted the Company's New Drug Application (NDA) under the accelerated approval pathway and granted Priority Review for avutometinib, an oral RAF/MEK clamp, in combination with defactinib, an oral, selective FAK inhibitor, in adult patients with recurrent KRAS mutant LGSOC and designated June 30, 2025, as the Prescription Drug User Fee Act (PDUFA) action date. The NDA was based on the positive, mature safety and efficacy data from the RAMP 201 trial as presented at the International Gynecologic Cancer Society (IGCS) 2024 Annual Meeting. The NDA also includes supportive data from the FRAME Phase 1 trial, the first study conducted with the combination therapy in recurrent LGSOC. These data underscore how avutometinib plus defactinib could address a significant unmet medical need among patients with recurrent LGSOC, if approved.

To further strengthen its positioning for a potential mid-2025 launch, Verastem previously announced agreements with Oberland Capital and IQVIA. The agreements with Oberland Capital include a debt refinancing and an equity investment, which strengthens the Company's cash position and will help fund commercialization past FDA approval and other pipeline programs. The strategic collaboration with IQVIA leverages IQVIA's world-class infrastructure and commercialization solutions to complement the Company's launch strategy in recurrent LGSOC.

Key Milestones Expected for 2025:

- Primary analysis from both the FRAME and RAMP 201 clinical trials will be published in H1 2025; submit RAMP 201 primary analysis publication for NCCN consideration in H1 2025.
- Present additional analyses from the RAMP 201 trial at a medical meeting in Q1 2025.
- Plan for FDA decision on approval of the combination of avutometinib plus defactinib in recurrent KRAS mutant LGSOC, expected by June 30, 2025.
- Complete enrollment for the international Phase 3 confirmatory RAMP 301 clinical trial for patients with recurrent LGSOC regardless of KRAS mutation status by the end of 2025.

- Report initial data from the RAMP 201J Phase 2 clinical trial being conducted in Japan with the Japanese Gynecologic Oncology Group (JGOG) evaluating the safety and efficacy of avutometinib in combination with defactinib for recurrent LGSOC in H2 2025.
- Continue to advance the regulatory pathway in Japan and Europe.

Maximize the Synergistic Potential of Avutometinib Plus Defactinib for Advanced Solid Tumor Market Expansion Opportunities

RAMP 205: Avutometinib Plus Defactinib in Combination with Chemotherapy in First-Line Metastatic Pancreatic Cancer

At the American Society of Clinical Oncology (ASCO) Annual Meeting in June 2024, Verastem presented initial interim data from the ongoing RAMP 205 Phase 1/2 clinical trial evaluating multiple dose cohorts of avutometinib plus defactinib in combination with gemcitabine and Nab-paclitaxel as first-line systemic treatment for patients with metastatic pancreatic cancer. Patients receiving the combination in the dose level 1 cohort achieved a confirmed overall response rate (ORR) of 83% (5/6). One dose-limiting toxicity (DLT) was observed in the dose level 1 cohort, and the dose level was subsequently cleared.

Key Milestones Expected for 2025:

- Report updated data from the ongoing RAMP 205 trial in Q1 2025 and present data at a medical meeting in mid-year 2025.
- Choose a Recommended Phase 2 Dose (RP2D) for trial expansion in H1 2025.

RAMP 203: Avutometinib Plus Defactinib in Combination with a KRAS G12C Inhibitor in Non-Small Cell Lung Cancer (NSCLC)

In December 2024, the Company announced preliminary clinical data for the triplet combination cohort of avutometinib and LUMAKRAS™ (sotorasib) plus defactinib in the RAMP 203 Phase 1/2 study in KRAS G12C mutant advanced NSCLC. No DLTs have been observed in the triplet combination.

Key Milestones Expected for 2025:

- Complete enrollment in the KRAS G12C inhibitor, prior-treated Stage 1 Part B cohort in Q1 2025. Continue to follow patients in both doublet cohorts (KRAS G12C inhibitor naïve and prior-treated) for safety and efficacy to determine if observed efficacy supports expanded enrollment.
- Complete enrollment and evaluate the safety and efficacy of the triplet combination in H1 2025.
- Present an interim update at a medical meeting in H2 2025.

Advance Novel, Early-stage Pipeline to Create Multiple Opportunities to Demonstrate Potentially Transformative Outcomes in RAS/MAPK Pathway-driven Cancers

VS-7375, an Oral KRAS G12D (ON/OFF) Inhibitor, in Advanced Solid Tumors

In July 2024, GenFleet Therapeutics began dosing several patients in a Phase 1/2 trial in China that is evaluating VS-7375 in patients with KRAS G12D-mutated advanced solid tumors. Verastem announced on January 14, 2025, that it has exercised its option early to license VS-7375 from GenFleet. In addition, the Company announced preliminary clinical data from the Phase 1 dose-escalation study conducted by GenFleet in China. In the study, VS-7375, demonstrated oral bioavailability, no dose-limiting toxicities across six dose levels, and several partial responses, including patients with pancreatic and lung cancers. Enrollment in the Phase 1 dose-escalation cohort is ongoing.

Key Milestones Expected for 2025:

- File an investigational new drug (IND) application in the U.S. for VS-7375 in Q1 2025.
- Initiate a Phase 1/2a trial in the U.S. by mid-2025.
- Share preclinical and clinical data from the Phase 1 study of VS-7375 in China in H1 2025.

Discovery/lead optimization continues for the second and third programs in the GenFleet collaboration.

nAbout the Avutometinib and Defactinib Combinatio

Avutometinib is an oral RAF/MEK clamp that potentially inhibits MEK1/2 kinase activities and 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 the MEK-only inhibitors.

Defactinib is an oral, selective inhibitor of focal adhesion kinase (FAK) and proline-rich tyrosine kinase-2 (Pyk2), the two members of the focal adhesion kinase family of non-receptor protein tyrosine kinases. FAK and Pyk2 integrate signals from integrin and growth factor receptors to regulate cell proliferation, survival, migration, and invasion. FAK activation has been shown to mediate resistance to multiple anti-cancer agents, including RAF and MEK inhibitors.

Verastem Oncology is currently conducting clinical trials with avutometinib with and without defactinib in RAS/MAPK-driven tumors as part of its **R**af **A**nd **M**ek **P**rogram or RAMP. Verastem is currently enrolling patients and activating sites for RAMP 301 (GOG-3097/ENGOT-ov81/NCRI) (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).

Verastem was granted Priority Review and a Prescription Drug User Fee Act (PDUFA) date of June 30, 2025, for its New Drug Application (NDA) 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. Verastem initiated a rolling NDA in May 2024 to the FDA and completed its NDA submission in October 2024. 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.

Verastem Oncology has established a clinical collaboration with Amgen to evaluate LUMAKRAS™ (sotorasib) in combination with avutometinib and defactinib in both treatment-naïve patients and in patients whose KRAS G12C mutant non-small cell lung cancer progressed on a G12C inhibitor as part of the RAMP 203 trial (NCT05074810). Verastem has received Fast Track Designation from the FDA for the triplet combination in April 2024. 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 the avutometinib and defactinib combination for the treatment of pancreatic cancer.

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. 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. Verastem plans to file a U.S. investigational new drug (IND) application for VS-7375 during the first quarter of 2025 and expects to initiate a Phase 1/2a study in mid-2025.

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 RAS/MAPK pathway-driven cancers. 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," "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 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 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 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; 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" 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, as well as the other information we file with the SEC. 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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