



Verastem Presents Avutometinib and Defactinib Combination Program Updates at the 5th Annual RAS-Targeted Drug Development Summit

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Preclinical and Clinical Presentations Include Update on FRAME Study Low-Grade Serous Ovarian Cancer Efficacy Data

BOSTON--(BUSINESS WIRE)--Sep. 28, 2023-- Verastem Oncology, (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with cancer, today announced the presentation of scientific background and clinical trial updates on the avutometinib and defactinib programs at the 5th Annual RAS-Targeted Drug Development Summit in Boston, Massachusetts. The updates are part of two oral presentations by Jonathan Pachter, PhD, Chief Scientific Officer and Louis Denis, MD, Chief Medical Officer at Verastem Oncology. The first presentation titled "Vertical Inhibition of RAS, RAF & MEK: Enhancing Antitumor Efficacy of KRAS G12C & G12D Inhibitors with RAF/MEK Clamp Avutometinib", includes scientific rationale for clinical combinations with avutometinib and defactinib in various RAS pathway-driven cancers. The second presentation titled, "Introducing Rational Combinations of RAF/MEK Clamp Avutometinib: Breakthrough Therapy Designation & Beyond," discusses novel combination treatment approaches and provides an overview of the avutometinib and defactinib clinical development program.

The clinical presentation includes updated FRAME study efficacy data showing an overall response rate (ORR) of 42% (11 of 26) in evaluable patients with low grade serous ovarian cancer (LGSOC) (n=26). Among patients with KRAS mutant LGSOC (n=12), the ORR was 58% (7 of 12), compared to patients with KRAS wild-type LGSOC (n=12), the ORR was 33% (4 of 12). Across all LGSOC patients, the median duration of response was 26.9 months (95% CI: 8.5-47.3) while median progression free survival (PFS) was 20.0 months (95% CI: 11.1-31.2). As of the July 2023 data cutoff date, 19% of patients (5 of 26) were still on study treatment with a minimum follow-up of 17 months.

"We are encouraged that the high rate and long duration of objective responses in the recurrent LGSOC cohort of the FRAME study continue to provide foundational proof-of-concept supporting Breakthrough Therapy Designation for the combination of avutometinib and defactinib," said Dan Paterson, President and Chief Executive Officer of Verastem Oncology.

The FRAME study, led by Professor Udai Banerji, MBBS, MD, DNB, PhD, FRCP, Deputy Director of the Drug Development Unit at The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust, is an ongoing investigator-sponsored trial evaluating avutometinib in combination with defactinib among patients with advanced solid tumors, including recurrent LGSOC. The Company recently reported results of Part A of RAMP 201 in recurrent LGSOC including confirmed ORR by blinded independent central review of 45% (13/29; 95% CI: 26%,64%) with a tolerable safety profile at the American Society of Clinical Oncology (ASCO) 2023 Annual Meeting. The median duration of response and median PFS from RAMP 201 Part A were not yet reached at the time of the ASCO 2023 presentation.

About Verastem Oncology

Verastem Oncology (Nasdaq: VSTM) is a development-stage 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 novel small molecule drugs that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth, including RAF/MEK inhibition and focal adhesion kinase (FAK) inhibition. For more information, please visit www.verastem.com.

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 pathway inhibition. In contrast to currently available MEK 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 inhibitors. The U.S. Food and Drug Administration granted Breakthrough Therapy designation for the combination of Verastem Oncology's investigational RAF/MEK clamp avutometinib, with defactinib, its FAK inhibitor, for the treatment of all patients with recurrent low-grade serous ovarian cancer (LGSOC) regardless of KRAS status after one or more prior lines of therapy, including platinum-based chemotherapy.

Verastem Oncology is currently conducting clinical trials with its RAF/MEK clamp avutometinib in RAS pathway-driven tumors as part of its (Raf And Mek Program). RAMP 301 is a planned Phase 3 confirmatory trial evaluating the combination of avutometinib and defactinib versus standard chemotherapy or hormonal therapy for the treatment of recurrent LGSOC. RAMP 201 is a Phase 2 registration-directed trial of avutometinib in combination with defactinib in patients with recurrent LGSOC and has completed enrollment in the dose optimization and expansion phases and is enrolling for low-dose evaluation. Verastem Oncology has established clinical collaborations with Amgen and Mirati to evaluate LUMAKRAS™ (sotorasib) and KRAZATI™ (adagrasib) in combination with avutometinib in KRAS G12C mutant NSCLC as part of the RAMP 203 and RAMP 204 trials, respectively. Supported by the "Therapeutic Accelerator Award" Verastem Oncology received from PanCAN, the Company is conducting RAMP 205, a Phase 1b/2 clinical trial evaluating avutometinib and defactinib with gemcitabine/nab-paclitaxel in patients with front-line metastatic pancreatic cancer.

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