Verastem Oncology Announces Efficacy and Safety Data of Avutometinib and Defactinib in Recurrent Low-Grade Serous Ovarian Cancer (LGSOC) in Heavily Pretreated Patient Population

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Planned Subgroup Analysis of RAMP 201 Data Showed Combination Demonstrated Robust Efficacy in Recurrent LGSOC Regardless of Number and Class of Prior Therapies Including After Poor Response to Prior Therapy

Late-Breaking Abstract Featured as an Oral Presentation during a Plenary Session at the Annual Global Meeting of the International Gynecologic Cancer Society

BOSTON--(BUSINESS WIRE)--Nov. 6, 2023-- Verastem Oncology (Nasdaq: VSTM) (the "Company"), a biopharmaceutical company committed to advancing new medicines for patients with cancer, announced today results of the efficacy and safety of avutometinib and defactinib in recurrent low-grade serous ovarian cancer (LGSOC) following prior systemic therapy. The results of this planned subgroup analysis of Part A of the Phase 2 RAMP 201 (ENGOT-ov60/GOG-3052) trial were presented as a late-breaking abstract in an oral presentation during a plenary session at the Annual Global Meeting of the International Gynecologic Cancer Society (IGCS 2023) November 5-7, 2023, in Seoul, Korea.

"Patients with recurrent LGSOC currently have no medicines approved by the U.S. Food and Drug Administration and limited treatment options for their disease," said Rachel Grisham, M.D., Section Head, Ovarian Cancer and Director, Westchester Gynecologic Medical Oncology at Memorial Sloan Kettering Cancer Center N.Y., and the lead U.S. investigator of RAMP 201. "The results from this analysis are encouraging as the combination of avutometinib and defactinib demonstrates robust efficacy in recurrent LGSOC irrespective of the number of prior therapies, and for most of which, response to previous therapy was poor."

This planned subgroup analysis was performed to assess efficacy (confirmed objective response rate (ORR) via blinded independent central review per RECIST v1.1) and safety in prior lines of therapy (LoT) (1-3 LoT, ≥4 LoT). The analysis also evaluated efficacy in the context of best response to most recent prior treatment in the metastatic/recurrent setting.

In the combination arm, the observed ORRs were consistent across patients who received 1-3 (45.5%, 5/11, 95% CI 17-77) and ≥4 lines of therapy (44.4%, 8/18, 95% CI 22-69). Prior to enrollment in RAMP 201, only 2/23 (8.7%) patients responded to their last prior treatment in the metastatic/recurrent setting, whereas the combination of avutometinib and defactinib yielded an ORR of 43.5% (10/23) in this subgroup. The safety profiles of avutometinib and defactinib were similar in the less and more heavily pretreated subgroups and both analyses were consistent with previously reported safety data. The majority of treatment-emergent adverse events were mild to moderate.

Initial results of RAMP 201 Part A, presented at the American Society for Clinical Oncology Annual Meeting in May 2023, demonstrated an ORR of 45% (13/29) and tumor shrinkage in 86% (25/29) of evaluable patients that were treated with the combination of avutometinib and defactinib. Safety and tolerability were favorable and consistent with previously reported data. As previously announced, Verastem Oncology intends to file for accelerated approval with the FDA for the combination of avutometinib and defactinib based on mature data from the RAMP 201 trial, together with the results of the investigator-initiated FRAME trial. The Company plans to initiate its Phase 3 confirmatory trial (RAMP 301) of avutometinib and defactinib in LGSOC versus standard of care (SOC) chemotherapy (pegylated liposomal doxorubicin, paclitaxel, topotecan) or hormone therapy (letrozole, anastrozole) before the end of the year.

Dr. Grisham is a paid consultant for Verastem Oncology.

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 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 (**R**af **A**nd **M**ek **P**rogram). RAMP 301 is a 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.

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.

Forward-Looking Statements Notice

This press release includes forward-looking statements about Verastem Oncology's strategy, future plans and prospects, including statements related to the potential clinical value of various of its clinical trials. 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. 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.

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 occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis or result in unmanageable safety profiles as compared to their levels of efficacy; 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 third-party payors (including government agencies) may not reimburse; that there may be competitive developments affecting our product candidates; that we may not attract and retain high quality personnel; that data may not be available when expected; that enrollment of clinical trials may take longer than expected; that our product candidates will experience manufacturing or supply interruptions or failures; 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; that our target market for our product candidates might be smaller than we are presently estimating; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the avutometinib license agreement; that we or our other collaboration partners may fail to perform under our collaboration agreements; 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 may not have sufficient cash to fund our contemplated operations; 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 Secura Bio, Inc. will achieve the milestones that result in payments to us under our asset purchase agreement with Secura Bio, Inc.; that we will be unable to execute on our partnering strategies for avutometinib in combination with other compounds; 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, 2022 as filed with the Securities and Exchange Commission (SEC) on March 14, 2023 and in any subsequent filings with the SEC. The forward-looking statements contained in this press release reflect Verastem Oncology's views as of the date hereof, and Verastem Oncology 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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