Updated Data from Part A of Verastem Oncology's RAMP 201 Trial Show an Objective Response Rate of 45% in Patients with Recurrent Low-Grade Serous Ovarian Cancer Treated with Avutometinib and Defactinib

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Data Build on Breakthrough Therapy Designation of the Combination of Avutometinib and Defactinib in Low-Grade Serous Ovarian Cancer

Clinically Meaningful Response Rates and Manageable Safety and Tolerability Profile Continue to be Demonstrated in Heavily Pretreated Patient Population Regardless of KRAS Status

Results to Be Presented in a Poster Discussion Session at the American Society of Clinical Oncology Annual Meeting

BOSTON--(BUSINESS WIRE)--May 25, 2023-- Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with cancer, today announced updated data from Part A of the ongoing registration-directed RAMP 201 (ENGOTov60/GOG3052) trial evaluating the safety and efficacy of avutometinib (VS-6766) alone and in combination with defactinib among patients with recurrent low-grade serous ovarian cancer (LGSOC).

In the RAMP 201 study, treatment with the combination of avutometinib and defactinib resulted in an objective response rate (ORR) of 45% (13/29) and tumor shrinkage in 86% (25/29) of evaluable patients. Safety and tolerability continued to be favorable and consistent with previously reported data. These data, which will be presented at the American Society of Clinical Oncology Annual Meeting, build on the Breakthrough Therapy Designation granted by the U.S. Food and Drug Administration (FDA) for the combination in recurrent LGSOC.

RAMP 201 is an international registration-directed Phase 2 study evaluating the safety and efficacy of avutometinib (VS-6766) alone and in combination with defactinib among patients with recurrent LGSOC. The key objectives of Part A (Selection Phase) of the RAMP 201 LGSOC study were to select avutometinib monotherapy or the combination of avutometinib and defactinib as the go forward regimen to be studied in Part B (Expansion Phase) of the study, and to assess efficacy in both KRAS mutant and KRAS wild type LGSOC. These data reinforce the selection of the combination of avutometinib (3.2 mg PO twice weekly 21/28 days) with defactinib (200 mg PO BID 21/28 days) as the go forward regimen regardless of KRAS status, and target enrollment has been achieved in both Part A and Part B.

“These results demonstrate avutometinib in combination with defactinib can deliver high response rates for patients with recurrent LGSOC with a promising safety profile to date,” said Dr. Susana Banerjee, MBBS, MA PhD, FRCP, global and lead investigator of the study, Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust and Team Leader in Women’s Cancers at The Institute of Cancer Research, London. “It is particularly encouraging to see extensive tumor shrinkage in women who have had several treatment lines, including prior MEK inhibitors. These latest findings suggest the combination may offer a new treatment option for women with this hard-to-treat cancer, and we are hopeful it will become the new standard of care.”

Updated Results of Avutometinib and Defactinib Combination in RAMP 201 Part A

In Part A of the RAMP 201 trial, 31 patients with recurrent LGSOC were treated with the combination of avutometinib and defactinib, of which 29 were evaluable for efficacy with a minimum follow-up of 12 months and 13 patients remain on study treatment.

Overall, patients were heavily pretreated with a median of 4 prior systemic regimens (up to 11), including prior platinum-based chemotherapy, endocrine therapy and bevacizumab in most patients and prior MEK inhibitor therapy in about 13% of patients. Confirmed objective response rates (ORR) by blinded independent central review of 45% (13/29; 95% CI: 26%-64%) were observed. Tumor shrinkage was observed in the majority of patients, 86% (25/29). Further, 3 out of 4 patients who received prior MEK inhibitors responded to the combination.

Among the patients with KRAS mutant LGSOC, the ORR was 60% (9/15) in the combination arm. Among the patients with KRAS wild type LGSOC, the ORR was 29% (4/14). The median time to response was 5.5 months (range 1.6-14.7 months). The median duration of response and median progression free survival have not been reached.

The safety profile was consistent with previously reported safety data. The most common treatment-related adverse events for the combination in all treated patients (n=81) were nausea and vomiting, diarrhea, blood creatine phosphokinase (CPK) increased, peripheral edema, vision blurred, dermatitis acneiform and rash, fatigue, and dry skin, most of which were mild to moderate. The discontinuation rate, due to ≥ 1 adverse event, was 12% in the trial overall to date (4.9% due to elevated blood CPK).

“There are currently no treatments that are FDA or EMA approved specifically for the treatment of LGSOC, and this is clearly an area of unmet need. These results indicate that the combination of avutometinib and defactinib shows promise as a tolerable treatment with impressive response rates for women with recurrent LGSOC. Importantly, high response rates were seen both in women with and without KRAS mutations,” said Rachel N. Grisham, M.D., Section Head, Ovarian Cancer and Director, Westchester Gynecologic Medical Oncology at Memorial Sloan Kettering Cancer Center NY, and the study’s principal US investigator. “We look forward to the future outcomes from this important trial and improving care for women with LGSOC.”

Regulatory Update

The Company plans to include mature data from RAMP 201, the Verastem sponsored clinical trial, and the investigator-sponsored FRAME study to support filing for accelerated approval. The Company is finalizing the design of a randomized confirmatory trial with the FDA, which is planned to begin in the second half of 2023.

Dr. Banerjee and Dr. Grisham have consulting relationships with Verastem Oncology.

About Avutometinib (VS-6766)

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. Avutometinib is currently in late-stage development.

In contrast to other 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 201 is a registration-directed trial of avutometinib alone and in combination with defactinib in patients with recurrent LGSOC. 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 Low-Grade Serous Ovarian Cancer (LGSOC)

LGSOC is a highly recurrent, chemotherapy-resistant cancer, associated with slow tumor growth and high mortality rate. Approximately 6,000 women in the U.S. and 80,000 worldwide are living with this disease. Mutations in the KRAS gene are present in 30% of cases of LGSOC. LGSOC is most often diagnosed in women between the ages of 45-55 years and has a median survival of approximately ten years. The majority of patients experience severe pain and complications as the disease progresses. Chemotherapy is the standard of care for this disease, with limited treatment options currently available.

About RAMP 201

Verastem Oncology has initiated a Phase 2 registration-directed trial evaluating avutometinib alone and in combination with defactinib in patients with recurrent LGSOC as part of RAMP (**R**af **A**nd **M**ek **P**rogram). RAMP 201 (ENGOTov60/GOG3052) is an international collaboration between the European Network of Gynaecological Oncological Trial groups (ENGOT) and the Gynecologic Oncology Group (GOG) and sponsored by Verastem Oncology. It 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 LGSOC. The first part of the study will determine the optimal regimen of either avutometinib monotherapy or in combination with defactinib in patients with recurrent LGSOC randomized 1:1 in each treatment arm. The determination of which regimen to take forward into the expansion phase of the trial will be made based on objective response rate data. The expansion phase of the study will examine efficacy and safety parameters of the regimen selected.

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 GOG Foundation, Inc. (www.gog.org)

The GOG Foundation, Inc. is a not-for-profit organization with the purpose of promoting excellence in the quality and integrity of clinical and translational scientific research in the field of gynecologic malignancies. The GOG Foundation is committed to maintaining the highest standards in clinical trials development, execution, analysis, and distribution of results. The GOG Foundation is the only clinical trialist group in the United States that focuses its research on patients with pelvic malignancies, such as cancer of the ovary (including surface peritoneal malignancies), uterus (including endometrium, soft tissue sarcoma, and gestational trophoblastic neoplasia), cervix, and vulva. The GOG Foundation is multi-disciplinary in its approach to clinical trials, and includes gynecologic oncologists, medical oncologists, pathologists, radiation oncologists, oncology nurses, biostatisticians (including those with expertise in bioinformatics), basic scientists, quality of life experts, data managers, and administrative personnel.

About the GOG Partners Program

Supported by industry, GOG Partners program is structured to work directly with pharmaceutical organizations and operate clinical trials outside the National Cancer Institute (NCI) framework. The GOG Partners program promotes the mission of the GOG Foundation dedicated to transforming the care in Gynecologic Oncology. By providing an alternative venue for patient accrual and site infrastructure support, GOG Partners has helped provide additional trials and opportunities for patients outside the national gynecologic clinical trials network.

About ENGOT (www.engot.esgo.org)

The European Network for Gynaecological Oncological Trial (ENGOT) groups is a research network of the European Society of Gynaecological Oncology and was founded in Berlin in October 2007. Currently, ENGOT consists of 21 trial groups from 31 European countries that perform cooperative clinical trials. ENGOT's ultimate goal is to bring the best treatment to gynecological cancer patients through the best science and enabling every patient in every European country to access a clinical trial.

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 timing of commencing and completing trials, including topline data reports, interactions with regulators and potential for additional development programs involving Verastem Oncology's lead compound. 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 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 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 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 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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