Verastem Oncology Announces Initiation of a Confirmatory Phase 3 Trial of Avutometinib and Defactinib in Recurrent Low-Grade Serous Ovarian Cancer

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RAMP 301 Is Evaluating the Combination of Avutometinib and Defactinib vs Investigator's Choice of Therapy

Reported Data from Part A of RAMP 201 Trial Show an Objective Response Rate of 45%, and Manageable Safety and Tolerability Profile with the Combination

Company Intends to Submit an Accelerated Approval New Drug Application to the U.S. Food and Drug Administration for the Combination Based on Breakthrough Therapy Designation and Mature Data from RAMP 201 and FRAME Trials

BOSTON--(BUSINESS WIRE)--Dec. 13, 2023-- Verastem Oncology (Nasdaq: VSTM) (the "Company"), a biopharmaceutical company committed to advancing new medicines for patients with cancer, announced today that it has initiated its international confirmatory Phase 3 RAMP 301 trial (GOG-3097; ENGOT-ov81/NCRI), evaluating the combination of avutometinib and defactinib versus standard chemotherapy or hormonal therapy for the treatment of recurrent low-grade serous ovarian cancer (LGSOC).

"Patients and treating physicians have advocated for more research and development in support of LGSOC. At Verastem Oncology, we are moving with urgency to offer a Phase 3 study specifically directed at this disease in an effort to address this need," said Dan Paterson, President and Chief Executive Officer, Verastem Oncology. "Based on our Breakthrough Therapy Designation, the initiation and expected progress of this trial, along with the FRAME study data and mature RAMP 201 data, we plan to file for Accelerated Approval in the first half of next year, moving us a significant step closer to addressing the treatment needs of patients living with LGSOC."

RAMP 301 is the confirmatory study required by the U.S. Food and Drug Administration (FDA) for the combination of avutometinib and defactinib to potentially receive full approval for the treatment of recurrent LGSOC. The Company intends to submit an Accelerated Approval New Drug Application (NDA) for the combination of avutometinib and defactinib based on mature data from the Company's Phase 2 registration-directed RAMP 201 trial, together with the results of the investigator-initiated FRAME trial. The company recently reported results of Part A of the RAMP 201 trial, including confirmed objective response rates (ORR) by blinded independent central review of 45% with a response rate and safety profile consistent with previous studies.

"LGSOC has a unique molecular, histologic, and clinical profile that differs dramatically from the most common type of ovarian cancer. Response rates to standard of care treatments are disappointing, and there are still no FDA approved treatments specifically for LGSOC," said Rachel Grisham, M.D., Section Head, Ovarian Cancer and Director, Gynecologic Medical Oncology at Memorial Sloan Kettering Cancer Center in Westchester, NY and RAMP 301 global lead investigator. "The combination of avutometinib and defactinib continues to show promise in recurrent LGSOC, and I am looking forward to leading this confirmatory trial with the goal of establishing a new standard of care for people with this rare form of ovarian cancer."

According to Professor Susana Banerjee, MBBS, MA, PhD, FRCP, Consultant Medical Oncologist and Research Lead for the Gynaecology Unit at The Royal Marsden NHS Foundation Trust, Team Leader in Women's Cancers at The Institute of Cancer Research, London, and lead European investigator of the RAMP 301 trial, "Based on my experience treating women with LGSOC, it's clear that we need better therapeutic options. I am pleased this Phase 3 trial, following the initial positive results from the Phase 2 RAMP 201 trial, is enrolling patients to potentially address the significant limitations we have seen with other available therapies."

RAMP 301 (GOG-3097; ENGOT-ov81/NCRI) is an international collaboration between The GOG Foundation, Inc. (GOG) and the European Network of Gynaecological Oncological Trial groups (ENGOT) sponsored by Verastem Oncology. The trial is expected to enroll 270 patients who will be randomized to either the combination of avutometinib and defactinib or investigator's choice chemotherapy (pegylated liposomal doxorubicin, paclitaxel, topotecan) or hormone therapy (letrozole, anastrozole). The primary endpoint is progression free survival (PFS) by Blinded Independent Central Review. Secondary endpoints include ORR, duration of response, disease control rate, safety and tolerability, patient reported outcomes, and overall survival. RAMP 301 is a global trial with enrollment open in the U.S. and planned enrollment in Canada, the United Kingdom, Europe, Australia, and Korea.

Dr. Grisham and Dr. Banerjee are paid consultants 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 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 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 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 35-57% 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 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 standard of 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 and the timing of commencing and completing trials and regulatory submissions. 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 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 labeling and other matters that could affect the 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 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 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; that we may not have sufficient cash to fund our contemplated operations; 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 our target market for our product candidates might be smaller than we are presently estimating; that Secura Bio, Inc. will fail to fully perform under the asset purchase agreement with Secura Bio, Inc., 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 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, 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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