Verastem Oncology Announces Design for Confirmatory Trial of Avutometinib and Defactinib in Recurrent Low-Grade Serous Ovarian Cancer

July 5, 2023

Randomized Phase 3 Trial (RAMP 301) Will Evaluate the Combination of Avutometinib and Defactinib vs Standard of Care Treatment; Study to Commence in 2H 2023

Recently Published 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 File for Accelerated FDA Approval for the Combination Based on Mature Data from RAMP 201 and the FRAME Trial

BOSTON--(BUSINESS WIRE)--Jul. 5, 2023-- Verastem Oncology (Nasdaq: VSTM) (the "Company"), a biopharmaceutical company committed to advancing new medicines for patients with cancer, announced today that it has finalized with the U.S. Food and Drug Administration (FDA) the design of its confirmatory Phase 3 trial to evaluate the combination of avutometinib and defactinib for the treatment of recurrent low-grade serous ovarian cancer (LGSOC). RAMP 301, a randomized global confirmatory trial, will evaluate the efficacy and safety of avutometinib and defactinib versus standard of care (SOC) chemotherapy and hormonal therapy in patients with recurrent LGSOC. RAMP 301 is expected to begin enrollment in the second half of this year.

RAMP 301 is the follow-up confirmatory study for full approval in recurrent LGSOC. The Company intends to file for Accelerated FDA Approval for the combination of avutometinib and defactinib based on mature data from the Company's Phase 2 registration-directed RAMP 201, together with the results of the investigator-initiated FRAME trial. The Company recently reported results of Part A of RAMP 201 including confirmed objective response rates (ORR) by blinded independent central review of 45% (13/29; 95% CI: 26%,64%) with a tolerable safety profile.

"We are pleased to partner with GOG and ENGOT and announce the final study design for RAMP 301, another important milestone in advancing our avutometinib and defactinib program and bringing us closer to addressing the unmet needs of patients living with LGSOC," said Brian Stuglik, Chief Executive Officer, Verastem Oncology. "This trial builds on the encouraging results of Part A of the RAMP 201 trial and our breakthrough therapy designation, after one or more prior lines of therapy, and we are committed to bringing the first FDA-approved therapy for LGSOC to patients as quickly as possible."

RAMP 301 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 will enroll approximately 270 patients who will be randomized to either the combination of avutometinib and defactinib or SOC chemotherapy (pegylated liposomal doxorubicin, paclitaxel, topotecan) or hormone therapy (letrozole, anastrozole). Selection of the SOC regimen will be based on the preference of the investigator. The primary endpoint is progression free survival (PFS) by Blinded Independent Central Review. Secondary endpoints include overall response rates, duration of response, disease control rate, safety and tolerability, patient reported outcomes and overall survival. The RAMP 301 trial will be led globally and in the U.S. by Rachel Grisham, MD, Section Head, Ovarian Cancer and Director, Gynecologic Medical Oncology at Memorial Sloan Kettering Cancer Center in Westchester, NY. Susana Banerjee, MBBS, MA PhD, FRCP, global and lead investigator of the RAMP 201 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, will be leading the RAMP 301 trial in Europe.

Financial Update

As of March 31, 2023, Verastem Oncology had cash and short-term investments of $111.2 million. With the net proceeds from the underwritten public offering completed in June 2023 of approximately $91.5 million after deducting estimated underwriting discounts and commissions and estimated offering expenses, the Company has pro-forma cash and short-term investments as of March 31, 2023 of approximately $202.7 million.

Recent historical operating expenses have ranged between $16.0M -- $20.0M per quarter, which the Company does not anticipate will change significantly in the near term as the RAMP 301 trial commences.

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 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, the timing of commencing and completing trials and the Company’s anticipated operating expenses. 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.

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

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