Verastem Oncology Presents Positive Updated RAMP 201 Data for Avutometinib and Defactinib Combination in Recurrent Low-Grade Serous Ovarian Cancer at the International Gynecologic Cancer Society (IGCS) 2024 Annual Meeting

October 17, 2024 at 1:00 AM EDT

Robust overall response rates observed (31% overall, 44% in KRAS mutant, 17% in KRAS wild-type) in patients whose cancer had progressed despite prior treatment with chemotherapy and/or MEK inhibitors and/or bevacizumab

Patients on avutometinib and defactinib achieved a median progression free survival of more than one year (12.9 months); 22 months in KRAS mutant population

The Company recently met with the FDA to review the mature data set and remains on track to complete the NDA submission in October 2024

Additional data to be presented at the IGCS meeting and during Company-hosted investor conference call and webcast today, October 17, 2024 at 4:30 pm EDT

BOSTON--(BUSINESS WIRE)--Oct. 17, 2024-- Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with cancer, today announced updated data from the Phase 2 RAMP 201 (ENGOTov60/GOG3052) clinical trial evaluating the combination of avutometinib, an oral RAF/MEK clamp, and defactinib, an oral, selective FAK inhibitor, in patients with recurrent low-grade serous ovarian cancer (LGSOC). The data were published as a late-breaking abstract and additional detailed findings will be presented today in an oral plenary session at the International Gynecologic Cancer Society (IGCS) 2024 Annual Meeting in Dublin, Ireland.

The primary analysis of the RAMP 201 trial, with a data cutoff of June 30, 2024, showed a confirmed overall response rate (ORR) by blinded independent central review (BICR) of 31% (34/109; 95% CI: 23-41) in all evaluable patients with measurable disease with approximately 12 months of follow up. Among patients with KRAS mutant (mt) LGSOC, the confirmed ORR was 44% (25/57; 95% CI: 31-58) and for patients with KRAS wild-type (wt) LGSOC the confirmed ORR was 17% (9/52; 95% CI: 8-30). The median duration of response (DOR) was 31.1 months (95% CI: 14.8-31.1) in all evaluable patients, with 31.1 months (95% CI: 14.8-31.1) in the KRAS mt population and 9.2 months (95% CI: 5.5-NE[i]) in the KRAS wt population. The median progression-free survival (PFS) was 12.9 months (95% CI: 10.9-20.2) in all evaluable patients, with 22 months (95% CI: 11.1-36.6) in the KRAS mt population and 12.8 months (95% CI: 7.4-18.4) in the KRAS wt population. The disease control rate (DCR) at 6 or more months was 61% in the total evaluable population, 70% in KRAS mt population and 50% in KRAS wt population. The updated data continue to demonstrate avutometinib in combination with defactinib is generally well-tolerated, with a 10% discontinuation rate due to adverse events (AEs) and no new safety signals were identified. The most common treatment-related AEs (all grades, grade ≥3) for the combination were nausea (67.0%, 2.6%), diarrhea (58.3%, 7.8%), and increased blood creatine phosphokinase levels (60.0%, 24.3%).

“The notable response rates and low discontinuation rate seen with the combination of avutometinib and defactinib are significant. These updated results confirm the potential of this new combination therapy to change practice and be the new standard for care for recurrent low-grade serous ovarian cancer, which previously had limited effective treatment options,” said Professor Susana Banerjee, M.B.B.S., M.A., Ph.D., F.R.C.P., Global 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.

Regulatory Update

A Type A meeting was recently held with the U.S. Food and Drug Administration (FDA), during which the Company aligned with the FDA on the Company’s plans to complete the New Drug Application (NDA) submission in October 2024 for adult patients with recurrent KRAS mt LGSOC, who received at least one prior systemic therapy, based on the mature data from the RAMP 201 trial. The Company plans to seek Accelerated Approval from the FDA and request Priority Review. At this time, the FDA did not recommend pursuing a KRAS wt indication under Accelerated Approval. This strategic approach allows the Company to potentially reach the market more efficiently while mapping out a path forward with the FDA for the KRAS wild-type indication, including leveraging data from the ongoing RAMP 301 Phase 3 trial. RAMP 301, which is currently enrolling patients with recurrent LGSOC regardless of KRAS mutation status, will serve as a confirmatory study for the initial indication and has potential to expand the indication regardless of KRAS mutation status.

“In the mature data from the RAMP 201 trial most patients achieved tumor reductions and a median progression-free survival that was greater than one year across both KRAS mutant and KRAS wild-type patient populations. These results reinforce our confidence in the potential of the combination of avutometinib and defactinib to change how patients with recurrent low-grade serous ovarian cancer are treated,” said John Hayslip, M.D., chief medical officer of Verastem Oncology. “Encouraged by the durable clinical benefit seen in KRAS wild-type patients in RAMP 201 and the poorer prognosis in this subset of patients that are treated with sub-optimal treatment choices today, we believe that this treatment combination will be the preferred treatment option for all subgroups of patients with recurrent low-grade serous ovarian cancer. We are committed to making the combination available to these patients, including working with the FDA to outline a path forward to expand the indication with additional data.”

“Now that we have the mature data from the RAMP 201 trial, we are on track to complete our NDA submission for recurrent KRAS mutant low-grade serous ovarian cancer in October,” said Dan Paterson, president and chief executive officer of Verastem Oncology. “We look forward to working with the FDA to potentially bring the first and only FDA-approved treatment specifically for patients with recurrent KRAS mutant low-grade serous ovarian cancer to the U.S. market in 2025.”

Conference Call and Webcast Information

Verastem will hold an investor conference call and webcast on October 17, 2024 at 4:30 p.m. EDT, to review the mature data from the RAMP 201 trial. To access the conference call, please dial (844) 763-8274 (local) or (412) 717-9224 (international) at least 10 minutes prior to the start time and ask to be joined into the Verastem Oncology conference call. A live audio webcast of the call, along with accompanying slides, will be accessible under "Events & Presentations" in the Investors & Media section of the company's website at www.verastem.com.

The Company expects to file a current report on Form 8-K with the Securities and Exchange Commission (SEC) later today, which will include a copy of the IGCS oral presentation and the presentation which the Company intends to use on the investor conference call and webcast.

About RAMP 201

RAMP 201 (ENGOTov60/GOG3052) 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 low-grade serous ovarian cancer. The first part of the study (Part A) determined the selection of the go forward regimen, which was the combination of avutometinib and defactinib versus avutometinib alone, based on overall response rates. The expansion phases of the trial (Parts B and C) are evaluating the safety and efficacy of the go forward regimen of avutometinib 3.2 mg twice weekly and defactinib 200 mg twice daily. The Part D portion of the trial is evaluating a low dose of avutometinib in combination with defactinib to inform individualized dose reduction.

About Low-Grade Serous Ovarian Cancer (LGSOC)

LGSOC is a rare ovarian cancer that is insidious, persistent and ultimately fatal. LGSOC is distinct and different from high-grade serous ovarian cancer (HGSOC) and requires different treatment. LGSOC is highly recurrent and less sensitive to chemotherapy compared to HGSOC. Approximately 6,000-8,000 women in the U.S. and 80,000 worldwide are living with this disease. LGSOC affects younger women with bimodal peaks of diagnosis at ages between 20-30 and 50-60 and has a median survival of approximately ten years. The majority of patients report a negative impact of LGSOC on their mental and physical health, fertility, and long-term quality of life. The current standard of care for this disease includes hormone therapy and chemotherapy, but there are no treatments specifically approved by the U.S. Food and Drug Administration to treat LGSOC.

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-only 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 MEK-only inhibitors.

Verastem Oncology is currently conducting clinical trials with avutometinib in RAS/MAPK driven tumors as part of its **R**af **A**nd **M**ek **P**rogram or RAMP. Verastem is currently enrolling patients and activating sites for RAMP 301 (NCT06072781) an international Phase 3 confirmatory trial evaluating the combination of avutometinib and defactinib, a selective FAK inhibitor, versus standard chemotherapy or hormonal therapy for the treatment of recurrent low-grade serous ovarian cancer (LGSOC). RAMP 201 (NCT04625270) is a Phase 2 registration-directed trial of avutometinib in combination with defactinib in patients with recurrent LGSOC and enrollment has been completed for the RAMP 201 trial.

Verastem initiated a rolling New Drug Application (NDA) submission in May 2024 to the U.S. Food and Drug Administration (FDA) for the investigational combination of avutometinib and defactinib in adults with recurrent KRAS mutant LGSOC who received at least one prior systemic therapy and expects to complete its NDA submission in the second half of 2024 with a potential FDA decision in the first half of 2025. The FDA granted Breakthrough Therapy Designation of the investigational combination of avutometinib and defactinib for the treatment of all patients with recurrent LGSOC after one or more prior lines of therapy, including platinum-based chemotherapy. Avutometinib alone or in combination with defactinib was also granted Orphan Drug Designation by the FDA for the treatment of LGSOC.

Verastem Oncology has established clinical collaborations with Amgen and Mirati to evaluate LUMAKRAS™ (sotorasib) in combination with avutometinib and defactinib and KRAZATI™ (adagrasib) in combination with avutometinib in KRAS G12C mutant NSCLC as part of the RAMP 203 (NCT05074810) and RAMP 204 (NCT05375994) trials, respectively. The RAMP 205 (NCT05669482), a Phase 1b/2 clinical trial evaluating avutometinib and defactinib with gemcitabine/nab-paclitaxel in patients with front-line metastatic pancreatic cancer, is supported by the PanCAN Therapeutic Accelerator Award. FDA granted Orphan Drug Designation to avutometinib and defactinib combination for the treatment of pancreatic cancer.

About Verastem Oncology

Verastem Oncology (Nasdaq: VSTM) is a late-stage development 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 RAS/MAPK-driven cancers, specifically novel small molecule drugs that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth, including RAF/MEK inhibition and FAK inhibition. For more information, please visit www.verastem.com and follow us on LinkedIn.

Forward-Looking Statements

This press release includes forward-looking statements about, among other things, Verastem Oncology's programs and product candidates, strategy, future plans and prospects, including statements related to, the scope and expecting timing for the completion of the NDA submission for the avutometinib and defactinib combination in LGSOC, the ongoing discussions with the FDA and the ability to obtain Accelerated Approval and Priority Review of the mature RAMP 201 data, the potential of the combination of avutometinib and defactinib to change the way patients with recurrent LGSOC are treated, the potential of the results of the RAMP 301 Phase 3 trial to expand the indication regardless of KRAS mutation status, the structure of our planned and pending clinical trials, the potential clinical value of various of the Company's clinical trials, including the RAMP 201, RAMP 205 and RAMP 301 trials, the timing of commencing and completing trials, including topline data reports, interactions with regulators, the timeline and indications for clinical development, regulatory submissions and the potential for and timing of commercialization of product candidates. 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.

Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause our actual results to

differ materially from those expressed or implied in the forward-looking statements we make. 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 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 the market opportunities of our drug candidates are based on internal and third-party estimates which may prove to be incorrect; 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, which may delay our development programs, including delays in submission or review by the FDA of our NDA submission in recurrent KRAS mutant LGSOC if enrollment in our confirmatory trial is not well underway at the time of submission, or that the FDA may require the Company to enroll additional patients in the Company's ongoing RAMP-301 confirmatory Phase 3 clinical trial prior to Verastem submitting or the FDA taking action on our NDA seeking accelerated approval; risks associated with preliminary and interim data, which may not be representative of more mature data, including with respect to interim duration of therapy data; 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 we may be unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our product candidates that require or would commercially benefit from such tests, or experience significant delays in doing so; that the mature RAMP 201 data and associated discussions with the FDA may not support the scope of our rolling NDA submission for the avutometinib and defactinib combination in LGSOC, including with respect to KRAS wild type LGSOC; 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 or our decisions regarding execution of such commercialization; that we may not have sufficient cash to fund our contemplated operations, including certain of our product development programs; 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 the total addressable and target markets for our product candidates might be smaller than we are presently estimating; that we or Secura Bio, Inc. (Secura) will fail to fully perform under the asset purchase agreement with Secura, 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 not be able to establish new or expand on existing collaborations or partnerships, including with respect to in-licensing of our product candidates, on favorable terms, or at all; 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, 2023 as filed with the Securities and Exchange Commission (SEC) on March 14, 2024 and in any subsequent filings with the SEC, which are available at www.sec.gov. 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.

[i] *NE = could not be estimated based on number of patients with loss of response*

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