# Verastem Oncology Receives Breakthrough Therapy Designation for VS-6766 with Defactinib in Recurrent Low-Grade Serous Ovarian Cancer

May 24, 2021

*Results of Early Trial Demonstrate 70% Overall Response Rate (ORR) in Patients with KRAS Mutant Tumors, 44% ORR in KRAS Wild-Type Tumors and 52% ORR in All Evaluable Patients with a Favorable Safety Profile*

BOSTON--(BUSINESS WIRE)--May 24, 2021-- Verastem, Inc. (Nasdaq:VSTM) (also known as Verastem Oncology), a biopharmaceutical company committed to advancing new medicines for patients battling cancer, today announced that the U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy designation for the combination of its investigational RAF/MEK inhibitor VS-6766, 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.

“Patients with low-grade serous ovarian cancer urgently need better solutions due to low response rates and tolerability issues associated with current therapies,” said Melissa Aucoin, CEO of the National Ovarian Cancer Coalition. “A Breakthrough Therapy designation in this disease is a significant step forward for the women who often, at a relatively young age, start a lengthy battle with this highly recurrent and impactful disease.”

The combination of VS-6766 with defactinib is being evaluated in the ongoing investigator-initiated Phase 1/2 FRAME trial. In the most recent read-out from the FRAME LGSOC cohort (n=24), the overall response rate (ORR) is 52% (11 of 21 response evaluable patients), with KRAS mutant ORR at 70% (7 of 10 response evaluable patients), KRAS wild-type ORR at 44% (4 of 9 response evaluable patients) and KRAS status undetermined ORR at 0% (0 of 2 response evaluable patients). The most common side effects seen in the study were rash, creatine kinase elevation, nausea, hyperbilirubinemia and diarrhea, most being NCI CTC Grade 1/2 and all were reversible. Several patients have been on therapy for more than one year, indicating the potential for a long duration of benefit.

“Breakthrough Therapy designation will facilitate our efforts to verify the robust and durable response and compelling safety profile of VS-6766 with defactinib that we have seen in patients with LGSOC and potentially bring a new therapy to these patients as quickly as possible,” said Brian Stuglik, CEO of Verastem Oncology. “The majority of LGSOC is RAS pathway-driven, and we are committed to exploring the potential for VS-6766 as a backbone therapy across RAS pathway-driven solid tumors.”

RAS is the most frequently mutated oncogene, occurring in 30% of human cancers.[1,2] These cancers are typically highly aggressive and recurrent, sending signaling commands through the RAS pathway. VS-6766 is a novel dual inhibitor of the RAF/MEK signaling pathway. With this unique dual mechanism of action, VS-6766 confers vertical inhibition of the RAS pathway in a single drug. Verastem Oncology is evaluating VS-6766 in combination with agents targeting other nodes in the RAS pathway as well as with agents targeting parallel pathways to address multiple cancer indications and mutations.

Breakthrough Therapy designation allows for the expedited development and review of drugs for serious or life-threatening conditions. The designation requires preliminary clinical evidence that demonstrates the drug or combination may have substantial improvement on at least one clinically relevant endpoint over available therapy.[3]

Verastem Oncology is currently evaluating the combination of VS-6766 alone and with defactinib in a Phase 2 registration-directed trial. RAMP 201 (**R**af **A**nd **M**ek **P**rogram) (ENGOTov60/GOG3052) is an adaptive two-part multicenter, parallel cohort, randomized, open label trial to evaluate the efficacy and safety of VS-6766 alone and in combination with defactinib in patients with recurrent LGSOC.[4]

**About Low Grade Serous Ovarian Cancer (LGSOC)**

Low-grade serous ovarian cancer (LGSOC) is a recurrent, chemotherapy-resistant cancer with a high mortality rate.[5] It comprises 5-10% of serous ovarian cancers and 6-8% of all ovarian cancers.[6] There are an estimated 6,000 patients in the U.S. and 80,000 worldwide living with this disease.[6] LGSOC is most often diagnosed in women between the ages of 45-55 years.[6] LGSOC has a median survival of approximately 10 years,[6] with 85% of patients experiencing recurrence[7] and enduring severe pain and complications as the disease progresses. Chemotherapy is the standard of care for this disease.[6]

**About the VS-6766/Defactinib Combination**

The combination of VS-6766 and defactinib has been found to be clinically active in patients with KRAS mutant tumors. In an ongoing investigator-initiated Phase 1/2 FRAME study, the combination of VS-6766 and defactinib is being evaluated in patients with LGSOC, KRAS mutant NSCLC and colorectal cancer (CRC). The FRAME study was expanded to include new cohorts in pancreatic cancer, KRAS mutant endometrioid cancer and KRAS-G12V NSCLC. Verastem Oncology is also supporting an investigator-initiated Phase 2 trial evaluating VS-6766 with defactinib in patients with metastatic uveal melanoma.

Verastem Oncology has initiated Phase 2 registration-directed trials of VS-6766 with defactinib in patients with recurrent LGSOC and in patients with recurrent KRAS-G12V mutant NSCLC as part of its RAMP (**R**af **A**nd **M**ek **P**rogram).

**About RAMP**

Verastem Oncology has initiated Phase 2 registration-directed trials evaluating the combination of VS-6766 alone and with defactinib in patients with

recurrent LGSOC and in patients with recurrent KRAS-G12V mutant NSCLC as part of its RAMP (**R**af **A**nd **M**ek **P**rogram).

RAMP 201 (ENGOTov60/GOG3052) is an adaptive, two-part multicenter, parallel cohort, randomized, open-label trial to evaluate the efficacy and safety of VS-6766 alone and in combination with defactinib in patients with recurrent LGSOC.[8] The first part of the study will determine the optimal regimen of either VS-6766 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.

RAMP 202 is an adaptive, two-part multicenter, parallel cohort, randomized, open-label trial to evaluate the efficacy and safety of VS-6766 alone and in combination with defactinib in patients with KRAS mutant NSCLC, following treatment with a platinum-based regimen and immune checkpoint inhibitor.[9] The first part of the study will determine the optimal regimen of either VS-6766 monotherapy or in combination with defactinib in patients with KRAS-G12V mutant NSCLC randomized 1:1 in each treatment arm. An exploratory arm of the initial phase of the study will evaluate other KRAS mutations. The determination of which regimen to take forward into the expansion phase of the trial will be made based on data from KRAS-G12V mutant patients. The second phase of the study will examine efficacy and safety parameters of the most effective regimen.

For more information, please visit www.RAMP201Study.com and www.RAMP202Study.com.

**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 the RAF/MEK/FAK combination, the potential benefits of Breakthrough Therapy designation and the timing of commencing and completing registration-directed trials for the RAF/MEK/FAK combination. 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 defactinib in combination with VS-6766; 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 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 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; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the VS-6766 license agreement; 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 we will be unable to execute on our partnering strategies for defactinib in combination with VS-6766; 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, 2020 as filed with the Securities and Exchange Commission (SEC) on March 18, 2021 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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