Verastem Oncology Announces Updated Investigator-Sponsored Phase 1/2 FRAME Study Data of VS-6766 with Defactinib in Low-Grade Serous Ovarian Cancer Showing Encouraging Response Rates and Progression-Free Survival Presented at ESMO 2021

September 19, 2021

- *Median progression-free survival (mPFS) across all patients treated with VS-6766 in combination with defactinib in the study is 23.0 months.*
- *11 of 24 (46%) patients treated with the combination achieved a confirmed partial response (PR). Of the 11 patients with KRAS mutant LGSOC, 7 (64%) achieved a confirmed PR.*
- *Combination continues to exhibit a favorable tolerability profile.*
- *Top-line results from the selection portion of Verastem's registration-directed Phase 2 RAMP 201 LGSOC study expected during the first half of 2022.*

BOSTON--(BUSINESS WIRE)--Sep. 19, 2021-- Verastem Oncology (Nasdaq:VSTM), a biopharmaceutical company committed to advancing new medicines for patients with cancer, today announced a mini oral presentation highlighting updated data from the ongoing investigator-sponsored Phase 1/2 FRAME study. The FRAME study, led by The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust, is investigating VS-6766, Verastem's RAF/MEK inhibitor, in combination with defactinib, its FAK inhibitor, in patients with low grade serous ovarian cancer (LGSOC). The findings will be presented at the European Society of Medical Oncology (ESMO) Congress 2021, taking place September 16-21, 2021.

"Low-grade serous ovarian cancer is a rare, slow-growing cancer that does not respond well to chemotherapy or hormone therapy, and disproportionately affects younger women. The results presented at ESMO this year show that VS-6766 combined with defactinib continues to demonstrate encouraging response rates in patients with LGSOC, including a 46% partial response rate across the overall patient population and a 64% partial response rate in patients with KRAS-mutated LGSOC, with manageable rates of side-effects," said Dr Susana Banerjee, MBBS, MA, PhD, FRCP, lead author of the presentation, Team Leader in Women's Cancers at The Institute of Cancer Research, London, and Consultant Medical Oncologist and Research Lead for The Royal Marsden NHS Foundation Trust Gynaecology Unit.

"It's particularly promising that the combination was also effective in patients who had previously received a MEK inhibitor. I am delighted that this drug combination has shown such encouraging results in a group of patients who urgently need new treatments."

"The investigator-sponsored FRAME study, the initial results of which led the U.S. Food and Drug Administration (FDA) to grant Breakthrough Therapy designation for the VS-6766 and defactinib combination in LGSOC, continues to be instrumental in providing the foundational data for safety, efficacy and durability in this novel combination for RAS pathway tumors," said Brian Stuglik, Chief Executive Officer of Verastem Oncology. "These data indicate that combining VS-6766 with defactinib results in promising response rates and median progression-free survival in patients who have already received MEK inhibitors. Verastem's company-sponsored, registration-directed Phase 2 RAMP 201 study evaluating VS-6766 both alone and in combination with defactinib in patients with recurrent LGSOC is ongoing and we look forward to reporting top-line results from the selection portion of the study during the first half of 2022."

Updated Phase 1/2 FRAME Study Results in Patients with LGSOC

Among the evaluable patients with LGSOC (n=24), the overall response rate (ORR) was 46% (11 of 24). Among the patients with KRAS mutant LGSOC (n=11), the ORR was 64% (7 of 11). Among the patients with KRAS wild type LGSOC (n=9), the ORR was 44% (4 of 9). Of the evaluable patients, 10 (42%) received previous MEK inhibitor therapy.

The mPFS across all patients was 23.0 months (95% CI: 10.6- not reached). As of the April 2021 data cutoff date, 13 of 24 patients (54%) remained on study.

For context, for other therapies studied in recurrent LGSOC, response rates have been between 6% and 26% and mPFS was between 7.2 and 13.0 months.[1,2]

In the FRAME study, the most common Grade 3/4 treatment-related adverse events (AEs) were creatine kinase elevation (12%), rash (8%), diarrhea (4%), mouth ulcer/mucositis/glossitis (4%) and hyperbilirubinemia (4%), with only one discontinuation due to AEs as of the data cutoff.

These updated data suggest that the novel, intermittent dosing schedule used in the FRAME study continues to show encouraging clinical activity in patients with recurrent LGSOC, including in patients previously treated with a MEK inhibitor. Expansion cohorts are also ongoing in pancreatic cancer, KRAS/BRAF mutant endometrioid cancer and KRAS-G12V NSCLC.

Details for the ESMO 2021 mini oral presentation are as follows:

Title: Phase I study of the combination of the dual RAF/MEK inhibitor VS-6766 and the FAK inhibitor defactinib: Results of efficacy in low grade serous ovarian cancer

Speaker: Dr Susana Banerjee, Team Leader in Women's Cancers at The Institute of Cancer Research, London, and Consultant Medical Oncologist and Research Lead for The Royal Marsden NHS Foundation Trust Gynaecology Unit

Presentation #: 725MO
Session: Mini oral – Gynaecological cancers
Date and Time: Sunday, September 19, 2021; 17:50-17:55 CEST

About the Phase 1/2 FRAME Study

The FRAME study is an open-label, investigator-initiated study that is designed to assess safety, dose response and preliminary efficacy of the VS-6766/defactinib combination in patients with KRAS mutant solid tumors, including low-grade serous ovarian cancer (LGSOC), non-small cell lung cancer (NSCLC) and colorectal cancer (CRC). The FRAME study is being led by Professor Udai Banerji, MBBS, MD, DNB, PhD, FRCP, Deputy Director of the Drug Development Unit at The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust, and is being conducted in the United Kingdom. In this study, VS-6766 was administered using a twice-weekly dose escalation schedule and is administered 3 out of every 4 weeks. Defactinib is administered using a twice-daily dose escalation schedule, also 3 out of every 4 weeks. Dose levels are assessed in 3 cohorts: cohort 1 (VS-6766 3.2mg, defactinib 200mg); cohort 2a (VS-6766 4mg, defactinib 200mg); and cohort 2b (VS-6766 3.2mg, defactinib 400mg). The recommended Phase 2 dose was determined to be cohort 1 (VS-6766 3.2mg, defactinib 200mg).

About RAMP 201

Verastem Oncology has initiated a Phase 2 registration-directed trial evaluating VS-6766 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 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.[3] 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.

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

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).

The U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy designation for the combination of Verastem Oncology's 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.

About Verastem Oncology

Verastem Oncology (Nasdaq: VSTM) (Verastem, Inc.) 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," "encouraging" 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; that we do not receive additional proceeds from the contingent payments negotiated in the sale of COPIKTRA; 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.

References

[1] Gershenson, et al. European Society for Medical Oncology 2019.

[2] Monk, et al. Journal of Clinical Oncology 2020

[3] Clinicaltrials.gov. A Study of VS-6766 v. VS-6766 + Defactinib in Recurrent Low-Grade Serous Ovarian Cancer With and Without a KRAS Mutation. Available at: https://clinicaltrials.gov/ct2/show/NCT04625270?cond=vs6766&draw=2&rank=1.

View source version on businesswire.com: https://www.businesswire.com/news/home/20210919005021/en/

Investors:
Ajay Munshi
Vice President, Corporate Development
+1 781-469-1579
amunshi@verastem.com

Sherri Spear
Argot Partners
+1 212-600-1902
sherri@argotpartners.com

Media:
Lisa Buffington
Corporate Communications
+1 781-292-4205
lbuffington@verastem.com

Source: Verastem Oncology