Verastem Oncology Initiates Phase 2 Registration-Directed Trial of VS-6766 and Defactinib in Recurrent Low-Grade Serous Ovarian Cancer

November 30, 2020

Previous Data from Investigator-Initiated Phase 1/2 Trial Show Encouraging Response Rates, Durability and a Favorable Safety Profile

Phase 2 Adaptive Trial Design to Evaluate VS-6766 Alone and in Combination with Defactinib

Verastem to Seek FDA Accelerated Approval, Pending Trial Outcome

BOSTON--(BUSINESS WIRE)--Nov. 30, 2020-- Verastem, Inc. (Nasdaq:VSTM) (also known as Verastem Oncology), a biopharmaceutical company committed to advancing new medicines for patients battling cancer, today announced the initiation of a Phase 2 registration-directed clinical trial of VS-6766, its RAF/MEK inhibitor, and defactinib, its FAK inhibitor, in patients with recurrent low-grade serous ovarian cancer (LGSOC).

“Results to date have demonstrated the clinical activity of VS-6766 and defactinib in KRAS mutant cancers, signaling potentially promising clinical results in low-grade serous ovarian cancer and in KRAS-G12V mutant non-small cell lung cancer,” said Brian Stuglik, Chief Executive Officer of Verastem Oncology. “The start of our registration-directed trial in recurrent LGSOC is a significant milestone in our work to develop the backbone of therapy for RAS driven tumors, an area of minimal therapeutic results, significant toxicity and limited treatment options.”

The Phase 2 study (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.[1] 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. Trial enrollment is underway in the United States with European sites to follow. Additional information about this study can be found here on ClinicalTrials.gov (NCT04625270). The Company previously announced its successful meeting with the Food and Drug Administration (FDA) in Q3 2020 and the FDA’s support of the Company’s development strategy and adaptive trial design for LGSOC.

According to Susana Banerjee, M.D., Ph.D., Medical Oncologist and Research Lead for the Gynaecology Unit at The Royal Marsden and Team Leader at The Institute of Cancer Research, London, Global and Lead European Investigator of this trial, “Based on my experience treating patients with low-grade serous ovarian cancer in the Phase 1/2 FRAME trial, I have seen firsthand the potential for the combination of VS-6766 and defactinib, particularly in KRAS mutated tumors, which may address the significant limitations we have seen with other therapeutic approaches. This trial will further explore the encouraging response rates, durability and safety profile of VS-6766 and defactinib demonstrated in early phase studies and enable us to evaluate VS-6766 alone and in combination with defactinib to address the unmet needs of women with this specific type of ovarian cancer.”

“LGSOC is a difficult to treat disease most often diagnosed in women between the ages of 45 to 55 years. [2] The majority of these patients experience a significant amount of pain and impact on their lives over a long period of time as response rates with current therapies have historically been low and the toxicity profiles of these agents make it difficult to keep patients on therapy,” said Rachel N. Grisham, M.D., Section Head, Ovarian Cancer and Director, Gynecologic Medical Oncology at Memorial Sloan Kettering Cancer Center in Westchester, NY and the study’s principal US investigator. “This trial represents an opportunity to further evaluate the potential for improved outcomes for patients with LGSOC.”

The launch of the trial follows the recent results of two clinical trials led by Professor Udai Banerji, Deputy Director of Drug Development at The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust. The first, a Phase 1 trial published in *The Lancet Oncology*, showed that VS-6766 could be effective against a range of KRAS-mutated tumor types, including lung and gynecological cancers.[3] The second, a Phase 1/2 trial presented at the American Association for Cancer Research (AACR) Annual Meeting 2020, showed the combination of a RAF/MEK and FAK inhibitor could be beneficial for patients with KRAS mutant 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.[2] It comprises 5-10% of serous ovarian cancers and 6-8% of all ovarian cancers.[2] There are an estimated 6,000 patients in the U.S. and 80,000 worldwide living with this disease.[5] LGSOC is most often diagnosed in women between the ages of 45-55 years.[2] LGSOC has a median survival of approximately 10 years,[2] with 85% of patients experiencing recurrence[6] and enduring severe pain and complications as the disease progresses. Chemotherapy is the standard of care for this disease.[2]

About VS-6766

VS-6766 is an oral small molecule inhibitor of the RAF/MEK signaling pathway. In contrast to other MEK inhibitors in development, VS-6766 blocks both MEK kinase activity and the ability of RAF to phosphorylate MEK. This unique mechanism allows VS-6766 to block MEK signaling without the compensatory activation of MEK that appears to limit the efficacy of other inhibitors.

About Defactinib

Defactinib (VS-6063) is an oral small molecule inhibitor of FAK and PYK2 that is currently being evaluated as a potential combination therapy for

various solid tumors. The Company has received Orphan Drug designation for defactinib in ovarian cancer in the US, EU and Australia. Preclinical research by Verastem Oncology scientists and collaborators at world-renowned research institutions has described the effect of FAK inhibition to enhance immune response by decreasing immuno-suppressive cells, increasing cytotoxic T cells, and reducing stromal density, which allows tumor-killing immune cells to enter the tumor.[7,8]

About the VS-6766/Defactinib Combination

RAS mutant tumors are present in ~30% of all human cancers, have historically presented a difficult treatment challenge and are often associated with significantly worse prognosis.[9] Challenges associated with identifying new treatment options for these types of cancers include resistance to single agents, [10] identifying tolerable combination regimens with MEK inhibitors and new RAS inhibitors in development addressing only a minority of all RAS mutated cancers.

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. Updated data from this study presented at the 2nd Annual RAS-Targeted Drug Development Summit in September 2020 demonstrated a 56% overall response rate and long duration of therapy among patients with KRAS-G12 mt LGSOC.[10] Based on an observation of higher response rates seen in NSCLC patients with KRAS-G12V mutations in the study, Verastem will also be further exploring the role of VS-6766 and defactinib in KRAS-G12V NSCLC. The FRAME study was expanded in August 2020 to include new cohorts in pancreatic cancer, KRAS mutant endometrial cancer and KRAS-G12V NSCLC.

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 and the timing of commencing a registration-directed trial 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 make additional draws under our debt facility or 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-Q for the period ended September 30, 2020 as filed with the Securities and Exchange Commission (SEC) on November 9, 2020 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

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[1] 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?term=vs-6766&draw=2&rank=1. Accessed November 24, 2020.

[2] Grisham, R. Low grade serous carcinoma of the ovary. Oncology. 2016. 30(7):650-652. Available at: https://www.cancernetwork.com/view/low-grade-serous-carcinoma-ovary. Accessed November 24, 2020.

[3] Verastem Press Release. Verastem Oncology Announces New Data Published in The Lancet Oncology Supports Potential of VS-6766 as Treatment for RAS Mutant Tumors. October 28, 2020. Available at: https://investor.verastem.com/news-releases/news-release-details/verastem-oncology-announces-new-data-published-lancet-oncology. Accessed November 24, 2020.

[4] Verastem Press Release. Verastem Oncology Announces Preliminary Data from Investigator-initiated Study Highlighting Clinical Activity of RAF/MEK and FAK Combination in KRAS Mutant Tumors Presented at the American Association for Cancer Research 2020 Virtual Annual Meeting. April 27, 2020. Available at: https://investor.verastem.com/news-releases/news-release-details/verastem-oncology-announces-preliminary-data-investigator. Accessed November 24, 2020.

[5] Slomovitz, Gourley, Carey, Malpica, Shih, Huntsman, Fader., Grisham et al, Low-Grade serous ovarian cancer: State of the Science; Gynecol Oncol; 2020.

[6] Corrado G, Salutari V, Palluzzi E, Distefano MG, Scambia G, Ferrandina G. Optimizing treatment in recurrent epithelial ovarian cancer. Expert Rev Anticancer Ther. 2017;17:1147-1158. doi: 10.1080/14737140.2017.1398088

[7] Chénard-Poirier, M. et al. Results from the biomarker-driven basket trial of RO5126766 (CH5127566), a potent RAF/MEK inhibitor, in RAS- or RAF-mutated malignancies including multiple myeloma. Journal of Clinical Oncology 2017: 35. 10.1200/JCO.2017.35.15_suppl.2506.

[8] ClinicalTrials.gov. Phase I Trial of VS-6063 and RO5126766. (FRAME). Available at: https://clinicaltrials.gov/ct2/show/NCT03875820. Accessed November 24, 2020.

[9] Baines, A. T., Xu, D., & Der, C. J. (2011). Inhibition of Ras for cancer treatment: the search continues. Future medicinal chemistry, 3(14), 1787–1808. https://doi.org/10.4155/fmc.11.121

[10] Verastem Press Release. Verastem Oncology Announces Presentation of Updated Phase 1/2 FRAME Study Data at the 2nd Annual RAS-Targeted Drug Development Summit. September 16, 2020. Available at: https://investor.verastem.com/news-releases/news-release-details/verastem-oncology-announces-presentation-updated-phase-12-frame. Accessed November 24, 2020.

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