



Verastem Oncology Initiates Phase 2 Registration-Directed Trial of VS-6766 and Defactinib in Previously Treated KRAS Mutant Non-Small Cell Lung Cancer

December 15, 2020

Phase 2 Adaptive Trial Design to Evaluate VS-6766 Alone and in Combination with Defactinib With a Focus on KRAS-G12V Mutations

Trial Designed to Address Significant Unmet Medical Need in These Treatment-Resistant Tumors

Verastem Oncology to Seek FDA Accelerated Approval, Pending Trial Outcome

BOSTON--(BUSINESS WIRE)--Dec. 15, 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, alone and in combination with defactinib, its FAK inhibitor, in patients with KRAS mutant non-small cell lung cancer (NSCLC).

"Currently available options for patients with KRAS mutant NSCLC are associated with minimal efficacy, as well as resistance and toxicity issues. Our study will further elucidate the impact of VS-6766, alone or in combination with defactinib, in overcoming these challenges to improve outcomes," said Brian Stuglik, Chief Executive Officer of Verastem Oncology. "Our VS-6766 and defactinib NSCLC development program's specific focus on G12V mutations is unique and represents a potentially significant step forward in understanding how we can deliver a better treatment option for these patients."

The RAMP 202 (Raf And Mek Program) study is a Phase 2, 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.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 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. Additional information about this study can be found [here](#) on [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT04620330).

"In this study, we hope to advance our understanding of a potential new option for patients with KRAS mutant NSCLC by targeting the RAF/MEK and FAK pathways," said D. Ross Camidge, M.D., Ph.D., Director of Thoracic Oncology at the University of Colorado School of Medicine and University of Colorado Cancer Center member and the study's U.S. principal investigator. "Some key advances have come from looking at specific KRAS mutations and by also focusing on G12V mutations, allowing us to build upon the areas that have shown particular promise and determine an optimal path forward."

"NSCLC, which constitutes over 80% of lung cancers,² is the single leading cause of cancer deaths worldwide² and approximately 25% of NSCLCs contain activating mutations in the RAS signaling pathway,"³ said Silvia Novello, M.D., Ph.D., Professor of Respiratory Medicine at the Department of Clinical and Biological Sciences of the University of Turin, Italy and EU principal investigator of the study. "Making progress with these mutated tumors is critical as they have proven extremely difficult to target with an effective and well-tolerated option and have, therefore, left patients with limited options and minimal results."

Verastem Oncology recently announced the initiation of its RAMP 201 Phase 2 registration-directed clinical trial of VS-6766 and defactinib, in patients with recurrent low-grade serous ovarian cancer.

About KRAS Mutant Non-Small Cell Lung Cancer (NSCLC)

Approximately 85% of lung cancers are non-small cell lung cancer (NSCLC),² which are the single leading cause of cancer deaths worldwide.² KRAS mutation occurs in approximately 25% of NSCLC adenocarcinoma patients.³ Two of the most common types of KRAS mutations are G12V, which are present in approximately 7% of NSCLC and G12C,⁴ which occur in approximately 13% of NSCLCs.⁵ There are several agents in development for KRAS-G12C mutations, but this study represents the first time that an agent will be studied specifically for KRAS-G12V. Studies suggest that these types of KRAS mutations differ in clinical characteristics and response to traditional treatments such as chemotherapy.⁶

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 the FAK and PYK2 signaling pathways that is currently being evaluated as a potential combination therapy for various solid tumors. Verastem Oncology has received Orphan Drug Designation for defactinib in ovarian cancer in the U.S., EU and Australia. Preclinical research by Verastem Oncology scientists and collaborators at world-renowned research institutions have 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 about 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,⁹ 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 recurrent low-grade serous ovarian cancer (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 mutant LGSOC.¹⁰ Based on an observation of higher response rates seen in NSCLC patients with KRAS-G12V mutations in the study, Verastem Oncology is also exploring the role of VS-6766 and defactinib in KRAS-G12V mutant NSCLC in its Phase 2 RAMP 202 (Raf And Mek Program) study. The FRAME study was expanded in August 2020 to include new cohorts in pancreatic cancer, KRAS mutant endometrial cancer and KRAS-G12V mutant 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 our Quarterly Report on Form 10-Q for the quarter 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 we do not assume and specifically disclaim 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 [Clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/NCT04620330?term=VS-6766&draw=2&rank=2). A Study of VS-6766 v. VS-6766 + Defactinib in Recurrent G12V or Other KRAS-Mutant Non-Small Cell Lung Cancer. Available at: <https://clinicaltrials.gov/ct2/show/NCT04620330?term=VS-6766&draw=2&rank=2>. Accessed December 15, 2020.
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- ⁵ American Cancer Society. Key Statistics for Lung Cancer. Available at: <https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html>. Accessed December 15, 2020.
- ⁶ Garassino, M. C. et al. Different types of K-Ras mutations could affect drug sensitivity and tumour behaviour in non-small-cell lung cancer. *Annals of Oncology*. 2011 Jan;22(1):235-237. doi: 10.1093/annonc/mdq680. PMID: 21169473.
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⁸ [ClinicalTrials.gov](https://clinicaltrials.gov). Phase I Trial of VS-6063 and RO5126766. (FRAME). Available at: <https://clinicaltrials.gov/ct2/show/NCT03875820>. Accessed December 15, 2020.

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¹⁰ Verastem Oncology 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 December 15, 2020.

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Source: Verastem, Inc.