Verastem Oncology and Amgen Partner to Evaluate VS-6766 in Combination with LUMAKRAS™ (sotorasib) in Patients with KRAS G12C-Mutant Non-Small Cell Lung Cancer

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Clinical Collaboration Will Assess Safety and Efficacy of More Complete Vertical Blockade Along RAS Pathway

BOSTON--(BUSINESS WIRE)--Sep. 20, 2021-- Verastem Oncology (Nasdaq:VSTM), a biopharmaceutical company committed to advancing new medicines for patients battling cancer, today announced a clinical collaboration agreement with Amgen to evaluate the combination of VS-6766, Verastem Oncology's investigational dual RAF/MEK inhibitor, with Amgen's KRAS G12C inhibitor LUMAKRAS ™ (sotorasib) in KRAS G12C-mutant non-small cell lung cancer (NSCLC).

The Phase 1/2 trial will evaluate the safety, tolerability and efficacy of VS-6766 in combination with LUMAKRAS™ in patients with KRAS G12C-mutant NSCLC who have not been previously treated with a KRAS G12C inhibitor as well as in patients who have progressed on a KRAS G12C inhibitor. The study will therefore investigate the potential benefits of a more complete vertical blockade of the RAS pathway with the combination of VS-6766 (RAF/MEK blockade) with LUMAKRAS™ (G12C inhibition) in KRAS G12C-mutant locally advanced or metastatic NSCLC.

"Recent data indicate that acquired resistance to KRAS G12C inhibitors in patients occurs predominantly through additional mutations in the RAS pathway, many of which may be addressed with a downstream inhibitor such as VS-6766,"[1] said Ramaswamy Govindan, M.D., Professor, Department of Medicine, Oncology Division at Washington University School of Medicine and lead investigator of the study. "This clinical study of VS-6766 and LUMAKRAS™ will build on preclinical data showing synergy between these two agents, including tumor regression through deeper blockade of ERK pathway signaling."[2]

"We are pleased to partner with Amgen on this important research that could potentially expand treatment options for patients with KRAS G12C-mutant NSCLC," said Brian Stuglik, CEO of Verastem Oncology. "This collaboration advances our strategy to fully explore the potential of VS-6766 as a backbone of therapy to treat RAS pathway-driven cancers."

Verastem Oncology expects to initiate the clinical trial with VS-6766 and LUMAKRAS™ by the end of 2021.

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

Approximately 85% of lung cancers are non-small cell lung cancer (NSCLC), which are the single leading cause of cancer deaths worldwide.[3] KRAS mutation occurs in approximately 25% of NSCLC adenocarcinoma patients.[4] Two of the most common types of KRAS mutations are G12C, which occurs in approximately 13% of patients with NSCLC adenocarcinoma, as well as G12V, which is present in approximately 7% of NSCLC.[5,6] Currently, there is a high unmet need in the second-line treatment of KRAS mutant NSCLC.[3,7]

About VS-6766

VS-6766 (formerly known as CH5126766 and RO5126766) is a unique 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. 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.[8]

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) clinical trials.

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 combination of VS-6766 and LUMAKRAS™ and the timing of commencing trials for the 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 VS-6766 in combination with LUMAKRAS™; 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 or Amgen may fail to perform under our collaboration 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 VS-6766 in combination with defactinib or LUMAKRAS™; 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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[4] Roman, Marta, et al. KRAS oncogene in non-small cell lung cancer: clinical perspectives on the treatment of an old target. *Molecular Cancer*. 2018;17:33.

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[6] American Cancer Society. Key Statistics for Lung Cancer. Available at: https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html. Accessed June 2021.

[7] Pakkala S, et al. Personalized therapy for lung cancer: striking a moving target. *JCI Insights*. 2018;3:3120858

[8] Verastem Oncology Press Release. Verastem Oncology Receives Breakthrough Therapy Designation for VS-6766 with Defactinib in Recurrent Low-Grade Serous Ovarian Cancer. May 24, 2021. Available at: https://investor.verastem.com/news-releases/news-release-details/verastem-oncology-receives-breakthrough-therapy-designation-vs. Accessed June 2021.

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