



Verastem Oncology Announces Presentation of Updated Phase 1/2 FRAME Study Data at the 2nd Annual RAS-Targeted Drug Development Summit

September 16, 2020

Preliminary Data on VS-6766 and Defactinib Combination Continues to Show Encouraging Response Rates, Durability and a Favorable Safety Profile in KRAS Mutant Low-Grade Serous Ovarian Cancer in Investigator-Initiated Trial

New Preclinical Data Demonstrating Synergy and Tumor Regression with G12C Inhibitors in Combination with VS-6766 and FAK Inhibitor In Vitro and In Vivo Also Presented

Management to Host Investor Conference Call Today at 8:00 AM ET

BOSTON--(BUSINESS WIRE)--Sep. 16, 2020-- Verastem, Inc. (Nasdaq:VSTM) (also known as Verastem Oncology), a biopharmaceutical company committed to advancing new medicines for patients battling cancer, today announced updated results from the ongoing investigator-initiated Phase 1/2 FRAME study evaluating VS-6766, its RAF/MEK inhibitor, in combination with defactinib, its FAK inhibitor, which demonstrated robust response rates, duration of response and a favorable safety profile in patients with low-grade serous ovarian cancer (LGSOC). These data will be presented in a virtual oral presentation today by Dr. Udai Banerji from The Institute of Cancer Research and The Royal Marsden at the 2nd Annual RAS-Targeted Drug Development Summit.

"Existing treatments for patients with LGSOC are limited by either 10-25% response rates and/or increased toxicities, leading to high discontinuation rates. The FRAME data being presented today continue to demonstrate that RAF/MEK inhibition combined with FAK inhibition is well tolerated with a 56% overall response rate (ORR) in patients with KRAS-G12 mutant LGSOC and a 41% ORR in the overall LGSOC population. These data are still actively maturing with more than half of the patients still on treatment as of the data cutoff date, and responses in this patient population tend to deepen over time," said Dan Paterson, President and Chief Operating Officer of Verastem Oncology. "The response rates from this expanded data set are highly encouraging, consistent with the prior positive data from this study, and continue to speak to the significant potential of the VS-6766/defactinib combination for patients battling LGSOC."

Verastem recently met with the Food and Drug Administration (FDA), and the FDA is supportive of the Company's adaptive study design for the planned Phase 2 registration-directed trials evaluating VS-6766 and defactinib in patients with recurrent LGSOC. Verastem expects to commence registration-directed clinical trials in both recurrent LGSOC and KRAS mutant non-small cell lung cancer by the end of 2020. Assuming a positive outcome from these registration-directed trials, Verastem expects to submit New Drug Applications to the FDA requesting accelerated approval for the VS-6766/defactinib combination in both LGSOC and KRAS mutant NSCLC.

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

Among the patients with LGSOC (n=17), the overall response rate (ORR) was 41% (7 of 17 patients), all partial responses (PRs). Among the patients with KRAS-G12 mutant LGSOC (n=9), the ORR was 56% (5 of 9 patients). Of the seven patients who responded, five had received one or more prior MEK inhibitors. In patients with KRAS mutant LGSOC receiving the recommended Phase 2 dosing (RP2D) regimen, the ORR was 50% (3 of 6 patients). The LGSOC cohort of the FRAME study remains ongoing, with 53% (9 of 17 patients) still on study as of the data cutoff date of August 17, 2020, with three patients on treatment for two years or more.

The most common Grade ≥ 3 treatment-related adverse events (TEAEs) observed for the recommended Phase 2 dosing regimen were rash (4%) and elevated creatine kinase (4%). No patients discontinued from the FRAME study due to TEAEs.

The novel, intermittent, combination dosing schedule used in the FRAME study continues to show encouraging clinical activity in patients with KRAS mutant LGSOC, including in patients who had previously progressed following treatment with a MEK inhibitor.

"These updated safety and efficacy results in both KRAS mutant LGSOC as well as the overall LGSOC population are highly encouraging. Of particular note in this early look at the data, is the strong, 50% response rate, durability, and tumor reduction seen in patients with KRAS mutant LGSOC receiving the recommended Phase 2 dosing (RP2D) regimen, which is the regimen we will be taking into our upcoming registration-directed study," said Brian Stuglik, Chief Executive Officer of Verastem Oncology. "With nine out of 11 patients at RP2D active in the study and responses still developing, we look forward to continued data outputs from this study and we remain on track to commence Phase 2 registration-directed trials in both LGSOC and KRAS mutant NSCLC by the end of this year."

Preclinical Results from Studies Investigating VS-6766 and Defactinib in Combination with G12C Inhibitors

KRAS-G12C inhibitors may benefit from novel combination approaches to enhance their inhibition of the ERK signaling pathway. In the preclinical results that will be presented today at the meeting, VS-6766 showed synergy with KRAS-G12C inhibitors in reducing cancer cell viability across a panel of KRAS-G12C mutant NSCLC and colorectal cancer (CRC) cell lines. This enhanced cellular anti-cancer activity of the combination correlated with deeper and more durable inhibition of ERK pathway signaling relative to G12C inhibition alone. In KRAS-G12C mutant NSCLC models in mice, the RAF/MEK dual inhibitor VS-6766 was more effective than trametinib when compared at equal dose level both alone and in combination with a G12C inhibitor. In the KRAS-G12C NSCLC models tested, the combination of G12C inhibitor with VS-6766 and FAK inhibitor induced tumor regressions of $\geq 30\%$ in all mice.

"The anti-tumor effects of VS-6766 were generally comparable to those of KRAS-G12C inhibitors in KRAS-G12C NSCLC models in mice and were stronger than the effects of trametinib at a comparable dose," said Jonathan Pachter, Ph.D., Chief Scientific Officer of Verastem Oncology. "The tumor

regressions observed with the triple combination of VS-6766, FAK inhibitor and G12C inhibitor were particularly striking. These data support clinical evaluation of VS-6766 and defactinib with G12C inhibitors in patients with KRAS-G12C mutant tumors.”

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 LGSOC, non-small cell lung cancer (NSCLC) and colorectal cancer (CRC). The FRAME study is being led by Dr. Banerji and is being conducted in the United Kingdom. In this study, VS-6766 was administered using a twice-weekly dose escalation schedule and was administered three out of every four weeks. Defactinib was administered using a twice-daily dose escalation schedule, also three out of every four weeks. Dose levels were assessed in three 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 VS-6766 3.2mg, defactinib 200mg. The FRAME study is now expanding to include new cohorts in pancreatic cancer, KRAS mutant endometrial cancer and KRAS-G12V mutant NSCLC.

Details for the RAS-Targeted Drug Development Summit oral presentation are as follows:

Title: Clinical Combinations: Dual RAF-MEK Inhibitor & FAK for Treatment of KRAS Mutant Cancers With a Focus on Low Grade Ovarian Cancer

Lead author: Udai Banerji, The Institute of Cancer Research and The Royal Marsden

Date and Time: Wednesday, September 16, 2020; 3:35 p.m. ET (12:35 p.m. PT)

Title: Synergistic Combinations with the Dual RAF/MEK Inhibitor VS-6766 to Overcome Resistance Mechanisms

Lead author: Jonathan Pachter, Verastem Oncology

Date and Time: Wednesday, September 16, 2020; 12:10 p.m. ET (9:10 a.m. PT)

Conference Call and Webcast Information

The Verastem Oncology management team will host a conference call and webcast on Wednesday, September 16, 2020, at 8:00 AM ET to discuss the updated Phase 1/2 FRAME study data. The call can be accessed by dialing (877) 341-5660 (US and Canada) or (315) 625-3226 (international), five minutes prior to the start of the call and providing the passcode 5278200.

The live, listen-only webcast of the conference call can be accessed by visiting the investors section of the Company's website at www.verastem.com. A replay of the webcast will be archived on the Company's website for 90 days following the call.

About VS-6766

VS-6766 (formerly known as CH5126766, CKI27 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.

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 and mesothelioma 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.^{1,2}

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. Challenges associated with identifying new treatment options for these types of cancers include resistance to single agents, 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 mt 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, KRASmt NSCLC and colorectal cancer (CRC). 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. 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, KRASmt 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-K for the year ended December 31, 2019 as filed with the Securities and Exchange Commission (SEC) on March 11, 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

¹ 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.

² <https://clinicaltrials.gov>, NCT03875820

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