Verastem Oncology Announces RAMP VS-6766 Clinical Trials and Corporate Updates

October 4, 2022

FDA Meeting Planned for Q4 to Discuss Regulatory Path Forward Based on Encouraging Results to Date in Ongoing RAMP 201 Trial in LGSOC

Results of Part A of RAMP 202 Trial in KRAS G12V-Mutant NSCLC Show VS-6766 ± Defactinib Did Not Meet Criteria to Continue to Expansion Phase

RAMP Trials with VS-6766 Combinations in KRAS G12C-Mutant NSCLC and Frontline Metastatic Pancreatic Cancer on Track

Newly Issued Patents Extend Coverage of VS-6766 and VS-6766 + Defactinib to 2038 and 2040

BOSTON--(BUSINESS WIRE)--Oct. 4, 2022-- Verastem Oncology (Nasdaq:VSTM), a biopharmaceutical company committed to advancing new medicines for patients with cancer, today announced an update on its RAMP (**R**af **A**nd **M**ek **P**rogram) clinical trials.

RAMP 201 in Patients with Recurrent Low Grade Serous Ovarian Cancer (LGSOC)

Verastem recently conducted a second planned interim analysis of the ongoing RAMP 201 trial among patients with recurrent LGSOC. Based on the results, including independently confirmed responses and no new safety signals, the Company is planning to meet with the U.S. Food and Drug Administration (FDA) in the fourth quarter to review the data set, discuss the go forward treatment regimen selection and align on a regulatory path forward.

"We are pleased with the encouraging results to date from our RAMP 201 trial in patients with recurrent low-grade serous ovarian cancer as we continue to see independently confirmed response rates, no new safety signals and a majority of patients still on treatment," said Brian Stuglik, Chief Executive Officer of Verastem Oncology. "As part of our Breakthrough Therapy Designation status and ongoing communications with the FDA, we look forward to our upcoming meeting to align on a regulatory path forward to advance this potential option for patients with LGSOC, who have a high unmet need and no approved therapies to treat their disease."

Since the first interim analysis announced in June, the trial has been continuing with all four cohorts (VS-6766 ± defactinib in KRAS mutant and KRAS wild type patient populations) with full enrollment based on the study protocol expected by the end of the year. Interim results will not be released at this time to ensure the integrity of this ongoing, registration-directed clinical trial.The Company will provide an update after the upcoming meeting with the FDA.

RAMP 202 in Patients with KRAS G12V-Mutant Non-Small Cell Lung Cancer

In a planned analysis of the Part A data from the RAMP 202 trial among patients with KRAS G12V NSCLC treated with the combination of VS-6766 and defactinib (n=19), the confirmed overall response rate (ORR) by independent review was 11% (2 of 19) with a disease control rate of 37%. The ORR with non-G12V KRAS mutations was 5% (2 of 37) (one confirmed and one unconfirmed by independent review) with a disease control rate of 54%, and no subtype was identified for further clinical evaluation of VS-6766 with defactinib in this trial. Verastem plans to present the Part A results of RAMP 202 at an upcoming medical congress.

"While this combination of VS-6766 and defactinib did not meet the pre-defined criteria to continue in the RAMP 202 trial, we remain optimistic about other combinations with VS-6766 in NSCLC," said Brian Stuglik, Chief Executive Officer of Verastem Oncology. "We will continue to analyze the results of the trial and include the findings in our development plans moving forward as we evaluate additional combinations for VS-6766 to best maximize its potential benefit."

RAMP 203 and RAMP 204 in Patients with KRAS G12C-Mutant NSCLC

The RAMP 203 Phase 1/2 trial to evaluate the safety, tolerability and efficacy of VS-6766 in combination with Amgen's KRAS G12C inhibitor LUMAKRAS™ (sotorasib) in patients with KRAS G12C-mutant NSCLC, has advanced to the Cohort 2 of 4mg VS-6766 in combination with 960mg of LUMAKRAS™. Initial results are expected by the fourth quarter of this year. The RAMP 204 Phase 1/2 trial of VS-6766 and Mirati's adagrasib, which will determine the maximum tolerated dose and recommended Phase 2 dose for the combination and evaluate the safety, tolerability and efficacy of the combination in patients who have progressed on a KRAS G12C inhibitor, is open and enrolling.

These studies will investigate the potential benefits of a more complete vertical blockade of the RAS pathway as acquired resistance to KRAS G12C inhibitors in patients occurs predominantly through additional mutations in the RAS pathway, many of which could be addressed with a downstream inhibitor such as VS-6766.

RAMP 205 in Patients with Frontline Metastatic Pancreatic Cancer

The Company plans to open the RAMP 205 Phase 1b/2 clinical trial of VS-6766 with defactinib in addition to standard of care chemotherapy (gemcitabine/nab-paclitaxel regimen) in frontline metastatic pancreatic cancer in the fourth quarter of this year. The trial, in partnership with the Pancreatic Cancer Action Network (PanCAN) will evaluate whether a more complete blockade of KRAS signaling, which is mutated in more than 90% of pancreatic cancer tumors, will improve outcomes for patients with pancreatic cancer.

Corporate Updates

Intermittent dosing intellectual property for both VS-6766 alone (previously announced) and in combination with defactinib was recently allowed,

extending patent coverage up to 2038 and 2040, respectively.

As of August 31, 2022, Verastem Oncology had cash, cash equivalents and investments of $110.4 million.

About VS-6766

VS-6766 is a RAF/MEK clamp that induces inactive complexes of MEK with ARAF, BRAF and CRAF potentially creating a more complete and durable anti-tumor response through maximal RAS pathway inhibition. VS-6766 is currently in late-stage development.

In contrast to other MEK inhibitors, 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 granted Breakthrough Therapy designation for the combination of Verastem Oncology's investigational RAF/MEK clamp 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.

Verastem Oncology is currently conducting clinical trials with its RAF/MEK clamp in RAS-driven tumors as part of its (**R**af **A**nd **M**ek **P**rogram). RAMP 201 is a registration-directed trial of VS-6766 alone and in combination with defactinib in patients with recurrent LGSOC. Verastem Oncology has established clinical collaborations with Amgen and Mirati to evaluate LUMAKRAS™ (sotorasib) and adagrasib in combination with VS-6766 in KRAS G12C mutant NSCLC as part of the RAMP 203 and RAMP 204 trials, respectively. As part of the "Therapeutic Accelerator Award" Verastem Oncology received from the Pancreatic Cancer Network (PanCAN), the Company is conducting RAMP 205, a Phase 1b/2 clinical trial evaluating VS-6766 and defactinib with gemcitabine/nab-paclitaxel in patients with front-line metastatic pancreatic cancer.

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 cash runway, the potential clinical value of various of its clinical trials, the timing of commencing and completing trials, including data reports, and potential for additional development programs involving Verastem Oncology's lead compound. 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 other compounds, including defactinib, LUMAKRAS™ and others; 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 our other collaboration partners may fail to perform under our collaboration agreements; 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 Secura Bio, Inc. will achieve the milestones that result in payments to us under our asset purchase agreement with Secura Bio, Inc.; that we will be unable to execute on our partnering strategies for VS-6766 in combination with other compounds; 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, 2021 as filed with the Securities and Exchange Commission (SEC) on March 28, 2022 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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