Verastem Oncology Granted Fast Track Designation for Combination of Avutometinib and Sotorasib for the Treatment of KRAS G12C-Mutant Non-Small Cell Lung Cancer (NSCLC)

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Ongoing RAMP 203 Trial Assessing a More Complete Vertical Blockade with RAF/MEK and KRAS G12C Inhibition Along RAS Pathway to Improve Outcomes in KRAS G12C-Mutant NSCLC

Confirmed Responses Observed in Both KRAS G12C Inhibitor Naïve and Pre-treated Patients in Initial RAMP 203 Trial Results; Enrollment Ongoing in Expansion Phase

BOSTON--(BUSINESS WIRE)--Jan. 18, 2024-- Verastem Oncology (Nasdaq:VSTM), a biopharmaceutical company committed to advancing new medicines for patients with cancer, today announced the U.S. Food and Drug Administration (FDA) has granted Fast Track Designation to Verastem Oncology's investigational RAF/MEK clamp, avutometinib, in combination with Amgen's KRAS G12C inhibitor, LUMAKRAS ™ (sotorasib), for the treatment of patients with KRAS G12C-mutant metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy and have not been previously treated with a KRAS G12C inhibitor. Fast Track is a process designed to facilitate the development and expedite the review of new drugs intended to treat or prevent serious conditions and address unmet medical need.

"Receiving Fast Track Designation for the combination of avutometinib and sotorasib reinforces the importance of improving the depth of MAPK pathway inhibition to enhance tumor regression relative to KRAS G12C inhibition alone and the potential of the combination of avutometinib and sotorasib in KRAS G12C mutant locally advanced or metastatic NSCLC," said Dan Paterson, President and CEO, Verastem Oncology. "Given that KRAS G12C is the most common KRAS mutation in NSCLC, the advancement of the combination is important in understanding potential new treatment approaches. We look forward to continued interaction with the FDA as we advance the development of this promising treatment regimen."

While newer targeted therapies specific to KRAS G12C-mutant NSCLC have shown significant promise, avutometinib targets the RAS pathway, which is a common source of acquired mutation. Preclinical proof-of-concept studies demonstrated improvements with the combination of avutometinib and sotorasib vs sotorasib alone, including deeper tumor regression through enhanced blockade of ERK activation and a decrease in the frequency of relapse of tumors. The RAMP 203 clinical development program will determine whether the promising preclinical results observed with the combination of avutometinib with sotorasib translate into improved clinical outcomes for patients with KRAS G12C-mutant locally advanced or metastatic NSCLC who have received prior therapy for metastatic disease and have not been previously treated with a KRAS G12C inhibitor.

Initial results of the RAMP 203 (NCT05074810) Phase 1/2, multicenter, open label, dose evaluation/expansion study evaluating the efficacy and safety of avutometinib + sotorasib 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 been previously treated with a KRAS G12C inhibitor demonstrated confirmed responses in both KRAS G12C inhibitor resistant and naïve patients. The pharmacokinetic profile of avutometinib in combination with sotorasib in the RAMP 203 trial was similar to results in monotherapy studies. No drug-drug interactions were observed between avutometinib and sotorasib. Avutometinib 4.0 mg PO BIW 21/28 days + sotorasib 960 mg PO QD 28/28 days was selected as RP2D based on dose limiting toxicity (DLT) assessment. These initial RAMP 203 results were presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in October, 2023. Enrollment of patients with KRAS G12C-mutant NSCLC who are either naïve to or previously treated with a KRAS G12C inhibitor is ongoing in the expansion phase of RAMP 203 with updated results expected in the first half of 2024.

About Avutometinib

Avutometinib 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. Avutometinib is currently in late-stage development.

In contrast to currently available MEK inhibitors, avutometinib blocks both MEK kinase activity and the ability of RAF to phosphorylate MEK. This unique mechanism allows avutometinib 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 avutometinib, 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 avutometinib in RAS pathway-driven tumors as part of its RAMP (**R**af **A**nd **M**ek **P**rogram) trials. RAMP 201 is a Phase 2 registration-directed trial of avutometinib in combination with defactinib in patients with recurrent LGSOC and has completed enrollment in the dose optimization and expansion phases and is enrolling for low-dose evaluation. Verastem Oncology has established clinical collaborations with Amgen and Mirati to evaluate LUMAKRAS™ (sotorasib) and KRAZATI™ (adagrasib) in combination with avutometinib in KRAS G12C mutant NSCLC as part of the RAMP 203 and RAMP 204 trials, respectively. Supported by the "Therapeutic Accelerator Award" Verastem Oncology received from PanCAN, the Company is conducting RAMP 205, a Phase 1b/2 clinical trial evaluating avutometinib and defactinib with gemcitabine/nab-paclitaxel in patients with front-line metastatic pancreatic cancer.

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 expected outcome and benefits of the collaboration with Genfleet, the potential clinical value of various of its clinical trials, the timing of commencing and completing trials, including topline data reports, interactions with regulators 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 avutometinib in combination with other compounds, including defactinib, LUMAKRAS™ and others; the uncertainties inherent in research and development, such as negative or unexpected results of clinical trials, the occurrence or timing of applications for our product candidates that may be filed with regulatory authorities in any jurisdictions; whether and when regulatory authorities in any jurisdictions may approve any such applications that may be filed for our product candidates, and, if approved, whether our product candidates will be commercially successful in such jurisdictions; 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 trial design, labeling and other matters that could affect the timing, 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 cause adverse safety events and/or unexpected concerns may arise from additional data or analysis, or result in unmanageable safety profiles as compared to their levels of efficacy; that our product candidates may experience manufacturing or supply interruptions or failures; that any of our third party contract research organizations, contract manufacturing organizations, clinical sites, or contractors, among others, who we rely on fail to fully perform; that we face substantial competition, which may result in others developing or commercializing products before or more successfully than we do which could result in reduced market share or market potential for our product candidates; 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, including as a result of conducting additional studies; that we may not have sufficient cash to fund our contemplated operations; that we may not attract and retain high quality personnel; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the avutometinib license agreement; that our target market for our product candidates might be smaller than we are presently estimating; that Secura Bio, Inc. will fail to fully perform under the asset purchase agreement with Secura Bio, Inc., including in relation to milestone payments; that we will not see a return on investment on the payments we have and may continue to make pursuant to the collaboration and option agreement with Genfleet or that Genfleet will fail to fully perform under the agreement; 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 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, 2022 as filed with the Securities and Exchange Commission (SEC) on March 14, 2023 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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