Verastem Oncology Announces Initial Results of RAMP 203 Trial of Avutometinib and LUMAKRAS™ (sotorasib) in KRAS G12C-Mutant Non-Small Cell Lung Cancer

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Avutometinib + Sotorasib Combination Demonstrated Preliminary Efficacy with Confirmed Responses in both KRAS G12C Inhibitor Resistant and Naïve Patients

No New Safety Signals Observed in Combination; Most Treatment-Related Adverse Events Mild to Moderate

Enrollment of Patients Naïve to or Previously Treated with a KRAS G12C Inhibitor Ongoing in Expansion Phase

BOSTON--(BUSINESS WIRE)--Oct. 14, 2023-- Verastem Oncology (Nasdaq: VSTM) (the "Company"), a biopharmaceutical company committed to advancing new medicines for patients with cancer, announced today the initial safety, pharmacokinetics and recommended Phase 2 dose (RP2D) in the RAMP 203 trial evaluating the safety, tolerability and efficacy of avutometinib in combination with sotorasib in patients with KRAS G12C-mutant non-small cell lung cancer (NSCLC). The results will be presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics October 11-15, 2023 in Boston, Massachusetts.

"The RAMP 203 study is investigating the potential benefits of a more complete vertical blockade of the RAS pathway with the combination of avutometinib and sotorasib in KRAS G12C-mutant locally advanced or metastatic NSCLC," said Mark Awad, M.D., Associate Professor of Medicine at Harvard Medical School and Director of Clinical Research of the Lowe Center for Thoracic Oncology at the Dana-Farber Cancer Institute, investigator on the trial, and presenting author. "These initial findings, including the recommended Phase 2 dose and the encouraging preliminary efficacy and safety results, provide support for the combination, and I look forward to completing the expansion phase of the trial."

RAMP 203 (NCT05074810) is a 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. The confirmed objective response rate (ORR) was 25% (3/12) across efficacy-evaluable patients and seen in both KRAS G12C inhibitor resistant (14.3%; 1/7) and naïve (40%; 2/5) patients.

The pharmacokinetic profile of avutometinib in combination with sotorasib 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. 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.

"The RAMP 203 trial builds on preclinical data which demonstrated the addition of avutometinib to sotorasib improved the depth of MAPK pathway inhibition and substantially enhanced tumor regression relative to sotorasib alone," said Dan Paterson, President and CEO, Verastem Oncology. "Given KRAS G12C mutations are the most common KRAS mutation in NSCLC and acquired mutations and amplifications occur upon clinical progression to KRAS G12C inhibitor monotherapy, the results of the RAMP 203 trial are important in understanding potential new treatment approaches for patients."

About the Avutometinib and Defactinib Combination

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 increased RAS pathway inhibition. 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 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 **R**af **A**nd **M**ek **P**rogram (RAMP). RAMP 301 is a Phase 3 confirmatory trial evaluating the combination of avutometinib and defactinib versus standard chemotherapy or hormonal therapy for the treatment of recurrent LGSOC. 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 potential clinical value of various of its clinical trials. 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 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 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 we may not attract and retain high quality personnel; 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, including as a result of conducting additional studies; that our target market for our product candidates might be smaller than we are presently estimating; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the avutometinib license agreement; that we or our other collaboration partners may fail to perform under our collaboration agreements; 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 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 avutometinib 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, 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 Verastem Oncology 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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Investors:
Dan Calkins
Investor Relations
+1 781-469-1694
dcalkins@verastem.com

Ryan Porter
Argot Partners
+1 212-600-1902
ryan.porter@argotpartners.com

Media:
Lisa Buffington
Corporate Communications
+1 781-292-4502
lbuffington@verastem.com

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