Verastem Oncology Announces Positive Initial Interim Safety and Efficacy Results from RAMP 205 Trial Evaluating Avutometinib Plus Defactinib in Combination with Gemcitabine and Nab-paclitaxel in First-Line Metastatic Pancreatic Cancer

May 23, 2024 at 5:01 PM EDT

83% (5/6) of patients achieved a confirmed partial response in cohort 1, the most mature dose level; one dose-limiting toxicity was observed, however, the dose level was subsequently cleared after additional patients were enrolled

Follow up of patients in the additional dose and schedule cohorts is ongoing to determine the recommended Phase 2 dose for study expansion

Poster presentation on Saturday, June 1, 2024 at the ASCO Annual Meeting

Company to host investor conference call and webcast on Friday, May 24, 2024 at 8:00 am EDT to discuss these data

BOSTON--(BUSINESS WIRE)--May 23, 2024-- Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with cancer, today announced the initial interim safety and efficacy results from the ongoing RAMP 205 Phase 1/2 clinical trial evaluating avutometinib plus defactinib in combination with gemcitabine and Nab-paclitaxel in the first-line in patients with metastatic pancreatic cancer. As of May 14, 2024, patients receiving the combination of avutometinib and defactinib with gemcitabine and Nab-paclitaxel in dose level 1 cohort achieved a confirmed overall response rate (ORR) of 83% (5/6), one dose-limiting toxicity (DLT) was observed in the dose level 1 cohort, and the dose level was subsequently cleared after additional patients were enrolled. The initial interim results will be presented at the upcoming American Society of Clinical Oncology (ASCO) Annual Meeting on June 1, 2024, in a poster session from 1:30-4:30 pm CDT in Chicago, IL.

“The initial interim results from the RAMP 205 trial evaluating avutometinib and defactinib in combination with standard of care first-line chemotherapy are encouraging and demonstrate the importance of targeting the RAS/MAPK pathway, as more than 90% of pancreatic tumors have a KRAS mutation. We continue to progress the study evaluating other dose and schedule regimens to determine the recommended Phase 2 dose in the trial,” said John Hayslip, M.D., chief medical officer of Verastem Oncology. "Metastatic pancreatic cancer continues to be a challenging cancer to treat and these data support the intent behind the Therapeutic Accelerator Award that we received from PanCAN to develop new therapies faster and more efficiently than in historical studies.”

“Verastem was the inaugural recipient of the PanCAN Therapeutic Accelerator Award, which has been an important part of PanCAN’s approach to advancing innovative treatments for pancreatic cancer,” said Anna Berkenblit, M.D., MMSc, Chief Scientific and Medical Officer at PanCAN. “We look forward to Verastem presenting their initial data from the Phase 1b/2a trial of avutometinib and defactinib in combination with standard care gemcitabine and Nab-paclitaxel in previously untreated metastatic pancreatic cancer at ASCO. There is a critical need for new treatment options in this disease, and we hope that the results from this study lead to improved outcomes for patients with pancreatic cancer.”

Initial Interim Data from RAMP 205 from the Ongoing Phase 1/2 Clinical Trial

As of a data cutoff of May 14, 2024, 41 patients had been treated in one of four dose and schedule cohort regimens of avutometinib and defactinib with gemcitabine and Nab-paclitaxel:

- In dose level 1, 6 patients received 2.4 mg of avutometinib twice a week (BIW), 200 mg of defactinib twice a day (BID) for 3 weeks out of every 4 and 800 mg/m^2 of gemcitabine and 125 mg/m^2 of Nab-paclitaxel on a schedule of day 1, day 8 and day 15.
- In dose level -1, 11 patients received 2.4 mg of avutometinib twice a week (BIW), 200 mg of defactinib twice a day (BID) for 3 weeks out of every 4 with 800 mg/m^2 of gemcitabine and 100 mg/m^2 of Nab-paclitaxel on a schedule of day 1, day 8 and day 15.
- In dose level 1a, 12 patients received 3.2 mg of avutometinib twice a week (BIW), 200 mg of defactinib twice a day (BID) for 3 weeks out of every 4 with 800 mg/m^2 of gemcitabine and 125 mg/m^2 of Nab-paclitaxel on a schedule of day 1 and day 15.
- In dose level 2a, 12 patients received 3.2 mg of avutometinib twice a week (BIW), 200 mg of defactinib twice a day (BID) for 3 weeks out of every 4 with 1000 mg/m^2 of gemcitabine and 125 mg/m^2 of Nab-paclitaxel on a schedule of day 1 and day 15.

As of May 14, 2024, in the dose level 1 cohort, 83% (5/6) of patients achieved a confirmed partial response with more than six months of follow-up at the time of data cutoff. Of the 26 patients in all cohorts who have had the opportunity to have their first scan while on treatment, 21 have experienced a reduction of the change in target lesion sum of diameters.

Patients in the trial had a median age of 64 years, 46% were male and 49% had an Eastern Cooperative Oncology Group (ECOG) Performance Status of one.

Initial Interim Safety Data from All Dose Cohorts

As of the May 14, 2024 data cutoff, 12 patients experienced 19 treatment emergent serious adverse events (SAEs), 11 patients with grade ≥3. Grade ≥3 treatment emergent SAEs included blood bilirubin increased (n=2), biliary obstruction (n=2), febrile neutropenia (n=2), pulmonary embolism (n=2), sepsis (n=2), anaemia (n=1), pneumoperitoneum (n=1), septic shock (n=1), skin infection (n=1), malignant neoplasm progression (n=1) and vomiting (n=1). Two patients discontinued treatment due to treatment emergent adverse events (febrile neutropenia, blood bilirubin increased, and detachment of retinal pigment epithelium).

One dose-limiting toxicity of febrile neutropenia was observed in the dose level 1 cohort and the dose cohort was cleared after additional patients were evaluated. In the additional dose cohorts enrolled more recently (-1, 1a, and 2a), follow up is ongoing and most patients remained on treatment at data cutoff.

Conference Call and Webcast Information

Verastem will hold an investor conference call and webcast on Friday, May 24 at 8:00 am EDT, to discuss these data. The call will feature members of Verastem's management team. To access the conference call, please dial (844) 763-8274 (local) or (412) 717-9224 (international) at least 10 minutes prior to the start time and ask to be joined into the Verastem Oncology conference call. A live audio webcast of the call, along with accompany slides, will be accessible here.

About Metastatic Pancreatic Cancer

Pancreatic cancer is the third leading cancer in the U.S. and seventh leading cause of cancer-associated mortality worldwide. Metastatic pancreatic cancer is defined as stage IV cancer, where the cancer spreads to other organs. In the U.S., over 30,000 patients are diagnosed with metastatic pancreatic cancer each year[1,2], for which the five-year survival rate is 3%[2]. Globally, over 240,000 patients are diagnosed with metastatic pancreatic cancer each year[3]. More than 90% of pancreatic cancers have a KRAS mutation[4]. The standard of care consists of surgery, chemotherapy, radiation or a combination of these approaches[5].

About RAMP 205 Phase 1/2 Study

RAMP 205 is a multicenter, open-label, single arm Phase 1b/2a study designed to evaluate the safety, tolerability and efficacy of avutometinib and defactinib in combination with standard of care chemotherapy (gemcitabine and Nab-paclitaxel) in patients with previously untreated metastatic pancreatic ductal adenocarcinoma. Part A of the study will evaluate different dose and schedule combinations to determine the recommended Phase 2 dose for expansion into Part B. RAMP 205 is supported by a PanCAN Therapeutic Accelerator Award.

About the Avutometinib and Defactinib Combination

Avutometinib is an investigational RAF/MEK clamp that is designed to induce inactive complexes of MEK with ARAF, BRAF and CRAF potentially creating a more complete and durable anti-tumor response through maximal RAS/MAPK pathway inhibition. Avutometinib is designed to block both MEK kinase activity and the ability of RAF to phosphorylate MEK. This differentiated proposed mechanism potentially allows avutometinib to block MEK signaling without the compensatory activation of MEK that appears to limit the efficacy of other MEK-only inhibitors. The U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy Designation of the investigational combination of avutometinib and defactinib, a selective 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. Avutometinib alone or in combination with defactinib was also granted Orphan Drug Designation by the FDA for the treatment of LGSOC.

Verastem Oncology is currently conducting clinical trials with avutometinib in RAS/MAPK driven tumors as part of its **R**af **A**nd **M**ek **P**rogram or RAMP. RAMP 301 (NCT06072781) is an international 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 (NCT04625270) is a Phase 2 registration-directed trial of avutometinib in combination with defactinib in patients with recurrent LGSOC and enrollment has been completed in each of the dose optimization and expansion phases and the low-dose evaluation.

Verastem Oncology has established clinical collaborations with Amgen and Mirati to evaluate LUMAKRAS™ (sotorasib) in combination with avutometinib and defactinib and KRAZATI™ (adagrasib) in combination with avutometinib in KRAS G12C mutant NSCLC as part of the RAMP 203 (NCT05074810) and RAMP 204 (NCT05375994) trials, respectively. The RAMP 205 (NCT05669482), a Phase 1b/2 clinical trial evaluating avutometinib and defactinib with gemcitabine/Nab-paclitaxel in patients with front-line metastatic pancreatic cancer, is supported by the PanCAN Therapeutic Accelerator Award.

About Verastem Oncology

Verastem Oncology (Nasdaq: VSTM) is a late-stage development 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 RAS/MAPK-driven cancers, specifically novel small molecule drugs that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth, including RAF/MEK inhibition and FAK inhibition. For more information, please visit www.verastem.com and follow us on LinkedIn.

Forward Looking Statements

This press release includes forward-looking statements about, among other things, Verastem Oncology's programs and product candidates, strategy, future plans and prospects, including statements related to the potential clinical value of various of the Company's clinical trials, including the RAMP 201, RAMP 205 and RAMP 301 trials, the timing of commencing and completing trials, including the RAMP 205 trial topline data reports, interactions with regulators, the potential for and timing of commercialization of product candidates 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. Forward-looking statements are not guarantees of future performance and are 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; the market opportunities of our drug candidates are based on internal and third-party estimates which may prove to be incorrect; 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 or that the FDA may require the Company to enroll additional patients in the Company's ongoing RAMP-301 confirmatory Phase 3 clinical trial prior to submitting an NDA seeking accelerated approval; 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 we may be unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our product candidates that require or would commercially benefit from such tests, or experience significant delays in doing so; 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 Therapeutics (Shanghai), Inc. (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, 2023 as filed with the Securities and Exchange Commission (SEC) on March 14, 2024 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20240523300933/en/

For Investor and Media Inquiries:
Julissa Viana
Vice President, Corporate Communications and Investor Relations
investors@verastem.com or
media@verastem.com

Source: Verastem Oncology