Verastem Oncology Exercises Option Early to License VS-7375, an Oral KRAS G12D (ON/OFF) Inhibitor, from GenFleet Therapeutics and Provides Preliminary Clinical Update on Phase 1 Study in China

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VS-7375 is a potential best-in-class oral and selective KRAS G12D (ON/OFF) inhibitor currently in Phase 1 development in China in advanced KRAS G12D mutant solid tumors; Verastem anticipates filing a U.S. IND application for VS-7375 during Q1 2025 and expects to initiate a Phase 1/2a study mid-2025

License establishes global development and commercialization rights for Verastem for VS-7375 outside of China, Hong Kong, Macau, and Taiwan

VS-7375 demonstrated oral bioavailability, no dose-limiting toxicities across six dose levels, and partial responses, including patients with pancreatic and lung cancers in preliminary clinical data from the Phase 1 dose-escalation study in China

BOSTON--(BUSINESS WIRE)--Jan. 14, 2025-- Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with RAS/MAPK pathway-driven cancers, today announced it has exercised early the option to license from GenFleet Therapeutics VS-7375 (also known as GFH375), a potential best-in-class oral and selective KRAS G12D (ON/OFF) inhibitor. In addition, the Company announced preliminary clinical data from the Phase 1 study being conducted by GenFleet in China.

As previously announced by GenFleet, 26 patients have been treated with VS-7375 in a Phase 1 dose-escalation study being conducted in China. Both confirmed and unconfirmed partial responses have been observed, including patients with metastatic pancreatic cancer and advanced non-small cell lung cancer. In addition, six dose cohorts have been cleared with no dose-limiting toxicities (DLTs) observed. In the study, oral dosing of VS-7375 has achieved plasma levels in patients that correlate with efficacious exposures that induced deep tumor regressions across all preclinical KRAS G12D tumor models as presented in collaboration with GenFleet at the AACR 2024 annual meeting.

Enrollment in the Phase 1 dose-escalation study in China is ongoing. Verastem remains on track to file a U.S. investigational new drug (IND) application for VS-7375 during the first quarter of 2025 and expects to initiate a Phase 1/2a study in mid-2025. The Companies expect to share updated preclinical and clinical data at upcoming medical meetings in mid-2025.

“Bringing VS-7375 formally into our pipeline allows us to leverage our scientific and development expertise in the RAS/MAPK-pathway to target KRAS G12D - the most prevalent KRAS mutation in human cancers,” said Dan Paterson, chief executive officer at Verastem Oncology. “Our decision to exercise the option early for VS-7375 was based on the safety, pharmacokinetics and efficacy data to date in the Phase 1 study in China, which are in line with our expectations and, importantly, indicate that patients are generally achieving oral bioavailability with exposures that correlate with strong tumor regressions across KRAS G12D mutant preclinical models. We look forward to building on the work GenFleet has started in China to bring VS-7375 to the clinic in the U.S. in mid-2025.”

In August of 2023, Verastem entered into a discovery and collaboration agreement with GenFleet to advance three oncology discovery programs targeting RAS pathway-driven cancers. The collaboration was designed with a risk-sharing structure and flexibility for Verastem to exclusively license up to three compounds selected for collaboration after the successful completion of pre-determined milestones in Phase 1 trials. Under the terms of the license for VS-7375, Verastem receives an exclusive global license to VS-7375 outside of the GenFleet markets of mainland China, Hong Kong, Macau, and Taiwan.

About VS-7375, an Oral KRAS G12D (ON/OFF) Inhibitor

VS-7375 is a potential best-in-class, potent, and selective oral KRAS G12D dual ON/OFF inhibitor. VS-7375 is the lead program from the Verastem Oncology discovery and development collaboration with GenFleet Therapeutics. GenFleet’s IND for VS-7375 (known as GFH375 in China) was approved in China in June 2024, and the first patient was dosed in a Phase 1/2 study in July 2024.

The Phase 1 portion of the study is being conducted in approximately 20 hospitals in China and will evaluate the safety and efficacy of VS-7375 in patients with advanced KRAS G12D mutant solid tumors. The Phase 1 study will determine the recommended Phase 2 dose (RP2D) and the Phase 2 will further evaluate the efficacy and safety of VS-7375 in patients with advanced solid tumors, such as pancreatic ductal adenocarcinoma, colorectal cancer, and non-small cell lung cancer.

Preclinical data presented at the American Association for Cancer Research (AACR) Annual Meeting in April 2024 demonstrated oral bioavailability across preclinical species, strong anti-tumor activity as a single agent, and potent efficacy in an intracranial tumor model suggesting the potential to treat brain metastases.

KRAS G12D represents 26% of all KRAS mutations, making it the most prevalent KRAS mutation in human cancers. The KRAS G12D mutation occurs most commonly in pancreatic (37%), colorectal (12.5%), endometrial (8%) and non-small cell lung (5%) cancers. Currently, no therapies are approved by the U.S. Food and Drug Administration targeting KRAS G12D.

About the GenFleet Therapeutics Collaboration

The collaboration with GenFleet Therapeutics aims to advance three oncology discovery programs related to RAS/MAPK pathway-driven cancers. The collaboration provides Verastem with an exclusive option to obtain a license for each of the three compounds in the collaboration after the successful completion of pre-determined milestones in a Phase 1 trial. Verastem selected VS-7375 (also known as GFH375), an oral KRAS G12D

(ON/OFF) inhibitor, as its lead program in December 2023 and the license for VS-7375 that was exercised in January 2025 is the first one from this collaboration. The licenses would give Verastem development and commercialization rights outside of the GenFleet markets of mainland China, Hong Kong, Macau, and Taiwan.

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 RAS/MAPK pathway-driven cancers. 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, FAK inhibition and KRAS G12D 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 anticipated timing for the IND application for VS-7375/GFH375, the expected outcome and benefits of its collaboration with GenFleet Therapeutics (Shanghai), Inc. (GenFleet), plans to initiate development studies outside of China, the timing of commencing and completing trials and compiling data, including topline data and reports, interactions with regulators, the expected timing of the presentation of data by the Company, the expected outcome and benefits of our collaboration with GenFleet Therapeutics, and the potential clinical value of various of the Company's 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.

Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause our actual results to differ materially from those expressed or implied in the forward-looking statements we make. 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-7375, 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 jurisdiction; whether and when regulatory authorities in any jurisdiction 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 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, which may delay our development programs, including delays in review by the FDA of our NDA submission in recurrent KRAS mutant; risks associated with preliminary and interim data, which may not be representative of more mature data, including with respect to interim duration of therapy data; that our product candidates may 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 the mature RAMP 201 data and associated discussions with the FDA may not support the scope of our NDA submission for the avutometinib and defactinib combination in LGSOC, including with respect to KRAS wild type LGSOC; 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 may 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 may take longer or cost more than planned, including as a result of conducting additional studies or our decisions regarding execution of such commercialization; that we may not have sufficient cash to fund our contemplated operations, including certain of our product development programs; that we may not attract and retain high quality personnel; that we or Chugai Pharmaceutical Co., Ltd. may fail to fully perform under the avutometinib license agreement; that the total addressable and target markets for our product candidates might be smaller than we are presently estimating; that we or Secura Bio, Inc. (Secura) may fail to fully perform under the asset purchase agreement with Secura, including in relation to milestone payments; that we may 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 may fail to fully perform under the agreement; that we may not be able to establish new or expand on existing collaborations or partnerships, including with respect to in-licensing of our product candidates, on favorable terms, or at all; 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 may not pursue or submit regulatory filings for our product candidates; and that our product candidates may 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, which are available at www.sec.gov. 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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