Mirati Therapeutics and Verastem Oncology Partner to Evaluate Adagrasib in Combination with VS-6766 in KRASG12C-Mutant Non-Small Cell Lung Cancer

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Clinical Collaboration to Support the Combination of KRAS^{G12C} Inhibitor Adagrasib with RAF/MEK Inhibitor VS-6766 to Establish Triple Blockade of the RAS Signaling Pathway

SAN DIEGO & BOSTON--(BUSINESS WIRE)--Nov. 22, 2021-- Mirati Therapeutics, Inc. (Nasdaq:MRTX), a clinical-stage targeted oncology company and Verastem Oncology (Nasdaq:VSTM), a biopharmaceutical company committed to advancing new medicines for patients battling cancer, today announced a non-exclusive clinical collaboration agreement to evaluate the combination of Mirati's investigational KRAS ^{G12C} inhibitor *adagrasib* with Verastem Oncology's investigational RAF/MEK inhibitor VS-6766 in KRAS ^{G12C}-mutant non-small cell lung cancer (NSCLC).

The primary objective of this multi-center, single-arm, open-label Phase 1/2 trial is to determine the maximum tolerated dose and recommended Phase 2 dose for the combination of *adagrasib* and VS-6766 in patients with KRAS^{G12C}-mutant NSCLC. The study will also investigate the safety, tolerability and efficacy of the combination in patients who have progressed on a KRAS^{G12C} inhibitor. The trial will build on preclinical data showing deeper blockade of ERK pathway signaling resulting in enhanced anti-tumor efficacy with the combination of *adagrasib* and VS-6766 relative to either agent alone.

"We are pleased to collaborate with Verastem Oncology on this clinical study of VS-6766 and *adagrasib*. We believe the data from this trial will help to better understand how these agents, when combined, could help improve patient outcomes," said James Christensen, Ph.D., chief scientific officer, Mirati Therapeutics, Inc. "This clinical collaboration is an example of how Mirati is aggressively advancing the study of *adagrasib* both as a monotherapy and in rational combinations as part of its expanding development portfolio to benefit people living with difficult-to-treat cancers."

"We continue to see evidence of the differentiated potential of the dual RAF and MEK properties and favorable safety profile of VS-6766 as an ideal combination therapy in treating RAS pathway-driven cancers. We are excited to partner with Mirati Therapeutics as part of our focused and rapidly advancing development strategy," said Brian Stuglik, CEO of Verastem Oncology. "Specifically, this collaboration will provide data on the potential of VS-6766 with *adagrasib* to provide deeper and more durable responses in patients with KRAS^{G12C}-mutant NSCLC by overcoming downstream resistance mechanisms in the RAS pathway to address unmet needs for NSCLC patients with KRAS^{G12C} mutations."

Under the terms of the agreement, Verastem Oncology and Mirati will have joint oversight of the study.

About KRAS Mutant Non-Small Cell Lung Cancer (NSCLC)

Approximately 85% of lung cancers are non-small cell lung cancer (NSCLC), which are the single leading cause of cancer deaths worldwide.[1] KRAS mutation occurs in approximately 25% of NSCLC adenocarcinoma patients.[2] Two of the most common types of KRAS mutations are G12C, which occurs in approximately 14% of patients with NSCLC adenocarcinoma, as well as G12V, which is present in approximately 7% of NSCLC adenocarcinoma.[3,4] Currently, there is a high unmet need in the second-line treatment of KRAS mutant NSCLC.[1,5]

About *Adagrasib* (MRTX849)

Adagrasib is an investigational, highly selective, and potent oral small-molecule inhibitor of KRAS^{G12C} that is optimized to sustain target inhibition, an attribute that could be important to treat KRAS^{G12C} mutated cancers, as the KRAS^{G12C} protein regenerates every 24-48 hours. Studies of *adagrasib* have shown that the drug has a long half-life, extensive tissue distribution and is well tolerated. *Adagrasib* has also shown single-agent responses in non-small cell lung cancer (NSCLC), colorectal cancer, pancreatic cancer, and other solid tumors with KRAS^{G12C} mutations. *Adagrasib* is a being evaluated in several clinical trials in combination with other anti-cancer therapies with strong scientific rationale in patients with advanced solid tumors. Registration-enabling studies are ongoing in NSCLC and colorectal cancer. For more information visit Mirati.com/science.

About VS-6766

VS-6766 (formerly known as CH5126766 and RO5126766) is a unique inhibitor of the RAF/MEK signaling pathway. In contrast to other MEK inhibitors in development, 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 (FDA) granted Breakthrough Therapy designation for the combination of Verastem Oncology's investigational RAF/MEK inhibitor 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.[6]

Verastem Oncology has initiated Phase 2 registration-directed trials of VS-6766 with defactinib in patients with recurrent LGSOC and in patients with recurrent KRAS-G12V mutant NSCLC as part of its RAMP (**R**af **A**nd **M**ek **P**rogram) clinical trials.

About Mirati Therapeutics, Inc.

Mirati Therapeutics Inc., is a clinical-stage biotechnology company whose mission is to discover, design and deliver breakthrough therapies to transform the lives of patients with cancer and their loved ones. The company is relentlessly focused on bringing forward therapies that address areas of high unmet need, including lung cancer, and advancing a pipeline of novel therapeutics targeting the genetic and immunological drivers of cancer. Mirati is using its scientific expertise to develop novel solutions in two registration-enabling programs: *adagrasib* (MRTX849), an investigational small molecule, potent and selective $KRAS^{G12C}$ inhibitor, as monotherapy and in combination with other agents, and *sitravatinib*, an investigational spectrum-selective inhibitor of receptor tyrosine kinases in combination with checkpoint inhibitor therapies. Mirati is also advancing its differentiated preclinical portfolio, including MRTX1133, an investigational $KRAS^{G12D}$ inhibitor, and other oncology discovery programs. Unified for patients, Mirati's vision is to unlock the science behind the promise of a life beyond cancer.

For more information about Mirati Therapeutics Inc., visit us at Mirati.com or follow us on Twitter and LinkedIn.

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.

Mirati Therapeutics, Inc. Forward Looking Statements

This press release contains forward-looking statements regarding the business of Mirati Therapeutics, Inc. ("Mirati"). Any statement describing Mirati's goals, expectations, financial or other projections, intentions or beliefs, development plans and the commercial potential of Mirati's drug development pipeline, including without limitation *adagrasib* (MRTX849), sitravatinib, MRTX1719 and MRTX1133, is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to risks and uncertainties, particularly those challenges inherent in the process of discovering, developing and commercialization of new drug products that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs.

Mirati's forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Mirati's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Mirati. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Mirati's programs are described in additional detail in Mirati's quarterly reports on Form 10-Q and annual reports on Form 10-K, which are on file with the U.S. Securities and Exchange Commission (the "SEC") available at the SEC's Internet site (www.sec.gov).These forward-looking statements are made as of the date of this press release, and Mirati assumes no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements, except as required by law.

Verastem Oncology 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 VS-6766 with *adagrasib*. 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 defactinib or *adagrasib* in combination with VS-6766; 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, Mirati Therapeutics or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under our license or other agreements; that we may not have sufficient cash to fund our contemplated operations; that we may be unable to make additional draws under our debt facility or obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that we will be unable to execute on our partnering strategies for defactinib or *adagrasib* in combination with VS-6766; 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, 2020 as filed with the Securities and Exchange Commission (SEC) on March 18, 2021 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.

[1] Molina, Julian R., Non–Small Cell Lung Cancer: Epidemiology, Risk Factors, Treatment, and Survivorship. National Institute of Health. Mayo Foundation for Medical Education and Research. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2718421/pdf/nihms121782.pdf. Accessed October 2021.

[2] Roman, Marta, et al. KRAS oncogene in non-small cell lung cancer: clinical perspectives on the treatment of an old target. *Molecular Cancer*. 2018;17:33.

[3] TCGA PanCancer Atlas (cBioPortal analysis).

[4] American Cancer Society. Key Statistics for Lung Cancer. Available at: https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html. Accessed October 2021.

[5] Pakkala S, et al. Personalized therapy for lung cancer: striking a moving target. *JCI Insights*. 2018;3:3120858

[6] Verastem Oncology Press Release. Verastem Oncology Receives Breakthrough Therapy Designation for VS-6766 with Defactinib in Recurrent Low-Grade Serous Ovarian Cancer. May 24, 2021. Available at: https://investor.verastem.com/news-releases/news-release-details/verastem-oncology-receives-breakthrough-therapy-designation-vs. Accessed October 2021.

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