Mirati announces Adagrasib (KRAZATI™) Receives Breakthrough Therapy Designation from FDA for Patients with Advanced, KRAS-Mutated Colorectal Cancer and NEJM Publishes Phase 1b/2 Data from Adagrasib With or Without Cetuximab in Colorectal Cancer

December 22, 2022

- U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation (BTD) for *adagrasib (KRAZATI™)* in combination with cetuximab in patients with KRAS^{G12C}-mutated advanced colorectal cancer (CRC) whose cancer has progressed following prior treatment with chemotherapy and an anti-VEGF therapy.
- Journal publication marks second New England Journal of Medicine (NEJM) inclusion in 2022 for *adagrasib.*

SAN DIEGO, Dec. 21, 2022 /PRNewswire/ -- Mirati Therapeutics, Inc. (NASDAQ: MRTX), announced today that the FDA has granted BTD to *adagrasib* in combination with cetuximab in patients with KRAS^{G12C}-mutated, advanced CRC whose cancer has progressed following prior treatment with chemotherapy and an anti-VEGF therapy. This designation is supported by results from the Phase 1b cohort of the KRYSTAL-1 trial.

The FDA program grants BTD to expedite the development and regulatory review of drugs that have demonstrated preliminary clinical evidence of a substantial improvement over available therapy in the treatment of patients with serious diseases on at least one clinically significant endpoint.

In addition, today, the NEJM published findings from the ongoing multicohort KRYSTAL-1 Phase 1/2 study evaluating *adagrasib* as monotherapy or combined with cetuximab in patients with KRAS^{G12C}-mutated metastatic colorectal cancer. These data reported promising clinical activity and demonstrated a favorable tolerability profile with reversible adverse events.

Summary of Clinical Results

- Of 28 evaluable patients, the combination of *adagrasib* and cetuximab demonstrated an objective response rate (ORR) of 46% (95% CI, 28 to 66); a median duration of response (DOR) of 7.6 months (95% CI, 5.7 to not estimable) and a median PFS of 6.9 months (95% CI, 5.4 to 8.1).
- The safety profile of *adagrasib* was consistent with previously reported safety findings; and the safety of the combination of *adagrasib* and cetuximab did not result in synergistic adverse events. Grade 3 or 4 treatment related adverse events (TRAEs) occurred in 34% of patients who received *adagrasib* monotherapy and in 16% of patients who received *adagrasib* and cetuximab in combination. No grade 5 TRAEs were observed.

"Preclinical studies and early clinical data indicate that the combination of a KRAS inhibitor and an anti-EGFR antibody could be an effective strategy to mitigate EGFR reactivation," said Rona Yaeger, M.D., Associate Attending Physician at Memorial Sloan Kettering Cancer Center and study author. "These results provide a strong rationale for continued development of this combination regimen."

"KRAS^{G12C}-mutations occur in 3-4% of colorectal cancers and are associated with poor outcomes.[1] Few effective treatment options exist for these patients," said Alan Sandler, M.D., Chief Medical Officer. "We are encouraged by this data, particularly *adagrasib* in combination with cetuximab. With the BTD status, we look forward to working together with the FDA to potentially bring this treatment option to late-line KRAS^{G12C}-mutant CRC patients through the accelerated approval pathway."

A Phase 3 trial evaluating *adagrasib* in combination with cetuximab in patients with KRAS^{G12C}-mutated colorectal cancer in the second line setting compared with standard chemotherapy (KRYSTAL-10; NCT04793958) is currently ongoing.

About KRAZATI™ (*adagrasib*)

In the U.S., KRAZATI was approved by the FDA for Accelerated Approval (Subpart H), which allows for the approval of drugs that treat serious conditions, and that fill an unmet medical need based on surrogate endpoints. KRAZATI was reviewed under the FDA Real-Time Oncology Review (RTOR) pilot program, which aims to explore a more efficient review process that ensures safe and effective treatments are made available to patients as early as possible. Mirati submitted a Marketing Authorization Application (MAA) in the EU in May 2022. In 2021, *adagrasib* achieved Breakthrough Therapy Designation in the U.S. as a potential treatment for patients with NSCLC harboring the KRAS^{G12C} mutation who have received at least one prior systemic therapy. For Prescribing Information, visit Mirati.com/KRAZATI_USPI

Adagrasib continues to be evaluated as monotherapy and in combination with other anti-cancer therapies in patients with advanced KRAS^{G12C}-mutated solid tumors, including NSCLC, colorectal cancer, and pancreatic cancer. For more information, visit Mirati.com/science.

Mirati has an Expanded Access Program (EAP) for *adagrasib* for the treatment of eligible patients with KRAS^{G12C}-mutated cancers, regardless of

tumor type, including patients with treated or untreated CNS metastases, in the U.S. Learn more about the EAP at Mirati.com/expanded-access-policy.

KRAZATI (*adagrasib*) U.S. Indication

KRAZATI is indicated for the treatment of adult patients with $KRAS^{G12C}$-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy.

This indication is approved under accelerated approval based on objective response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of a clinical benefit in a confirmatory trial(s).

About Mirati Therapeutics, Inc.

Mirati Therapeutics, Inc. is a 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. Unified for patients, Mirati's vision is to unlock the science behind the promise of a life beyond cancer.

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

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* (selective $KRAS^{G12C}$ inhibitor), *sitravatinib* (TAM receptor inhibitor), MRTX1719 (MTA-cooperative PRMT5 inhibitor), MRTX0902 (SOS1 inhibitor), and MRTX1133 (selective $KRAS^{G12D}$ inhibitor), 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.

Dr. Yaeger has a consulting relationship with Mirati Therapeutics.

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References

Fakih M, Tu H, et al. Real-World Study of Characteristics and Treatment Outcomes Among Patients with KRAS p.G12C-Mutated or Other KRAS Mutated Metastatic Colorectal Cancer. *The Oncologist.* 2022;27(8):663-674

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