December 21, 2015

Mirati Therapeutics Initiates Glesatinib (MGCD265) Phase 2 Trial In Non-Small Cell Lung Cancer (NSCLC)

Study Enrolling NSCLC Patients with Genetic Alterations of the MET Gene

Company Announces Proposed Generic Name of "Glesatinib" for MGCD265

SAN DIEGO, Dec. 21, 2015 /PRNewswire/ -- Mirati Therapeutics, Inc. (NASDAQ: MRTX) today announced that the Phase 2 clinical trial of glesatinib (MGCD265) has commenced. The Company also announced that "glesatinib" is the proposed generic name for MGCD265. Glesatinib is an inhibitor of the MET and Axl receptor tyrosine kinase pathways which, when altered, are drivers of tumor growth. The Phase 2 clinical trial will evaluate glesatinib in NSCLC patients with activating genetic alterations of the MET gene, including MET gene amplification and MET mutations.

"MET is a proto-oncogene that is widely recognized as an important mediator of uncontrolled growth in certain types of cancer. Alterations involving the MET gene locus, such as gene amplification and mutations, are implicated in the pathogenesis of non-small cell lung cancer and other solid tumors," said Pasi Janne, M.D., Ph.D., director, Lowe Center for Thoracic Oncology, Dana Farber Cancer Institute. "Glesatinib has demonstrated early signs of clinical activity in MET- or Axl-positive patients and warrants further study. I look forward to being the principal investigator for the Phase 2 glesatinib trial that could lead to improved treatment options for the significant number of non-small cell lung cancer patients with these MET alterations."

"In the ongoing Phase 1b dose expansion trial, glesatinib has demonstrated confirmed partial responses and significant tumor regressions in heavily pre-treated non-small cell lung cancer patients with MET or Axl gene amplification and MET mutations," said Charles M. Baum, M.D., Ph.D., president and CEO of Mirati. "The initiation of this Phase 2 trial is a significant milestone for Mirati and we look forward to demonstrating the potential therapeutic benefit to lung cancer patients with MET-driven tumors."

Glesatinib (MGCD265) Phase 2 Trial

The Phase 2 open-label, single-agent, multi-national trial will be conducted at up to 140 clinical trial sites. The purpose is to evaluate the safety and efficacy of glesatinib in NSCLC patients with MET gene alterations, which are known oncogenic drivers. Eligible patients must have failed at least one prior treatment with a platinum-based chemotherapy regimen. The trial will enroll patients with MET gene amplification or MET mutations (including exon-14 deletion mutations). The primary endpoint of the study is Objective Response Rate and the secondary endpoint is Progression Free Survival. Additional information about this Phase 2 clinical trial of glesatinib is available at www.clinicaltrials.gov using identifier: NCT02544633.

In separate press releases issued today, Mirati announced collaboration agreements with two advanced molecular diagnostic companies for the glesatinib development program.

Mirati anticipates providing a detailed update on the ongoing glesatinib Phase 1b dose expansion cohort at a scientific/medical conference taking place in the first half of 2016.

About NSCLC

Despite available treatment options, the overall five year survival rate for patients with NSCLC is only 17.8% and NSCLC results in the greatest number of cancer deaths in the U.S. Moreover, the five year overall survival rate for Stage 4 metastatic disease is a mere 4.0% (SEER Lung and Bronchus Cancer-2011). Over recent years, new therapies have been approved that target gene pathways implicated in progression of NSCLC, including EGFR kinase inhibitors, EML4-ALK inhibitors, VEGF monoclonal antibodies and PD-1 inhibitors. However, these targets represent only a fraction of the growing list of cancer genes that play a role in NSCLC. Given these factors, there remains a significant unmet medical need to develop new therapies that inhibit multiple targets, particularly those that also inhibit novel targets for which no therapy exists.

MET is highly expressed in NSCLC tumors and higher MET receptor expression rates correlate with advanced stages of tumor progression, and poor clinical outcomes. Recent data indicate that MET is a driver of tumor growth when it is genetically altered and activated by point mutations, exon 14 deletions, and gene amplification in a significant fraction (6-
7% of NSCLC patients. MET exon 14 deletion mutations and MET amplification were recently identified in a significant number of patients with lung adenocarcinoma in The Cancer Genome Atlas consortium project (TCGA-2014a) and through genomic profiling data from Foundation Medicine. MET mutations, including exon 14 deletion mutations, and MET gene amplification each exhibit the key characteristics of driver oncogenes in NSCLC. Additionally, rearrangements and amplification of the AXL tyrosine kinase gene appear to be drivers of tumor growth and occur in up to 2% of patients with NSCLC.

Extensive preclinical and clinical data indicate that activation of the MET pathway can result in resistance to EGFR inhibitors, including the third-generation EGFR inhibitors that are active against tumors with T790 mutations. Resistance is mediated through gene amplification and/or overexpression of alternative receptor tyrosine kinase (RTK) targets and pathways, including MET and Axl. In certain tumors, MET may actually substitute for, or cooperate with, EGFR to drive tumor growth and progression. MET activation is believed to mediate resistance to EGFR inhibitors by bypassing EGFR dependence and activating downstream signaling. In this setting, MET activation and EGFR mutations function as co-oncogenic drivers.

**About Glesatinib (MGCD265)**

Glesatinib (MGCD265) is a tyrosine kinase inhibitor that is expected to potently and selectively target tumors in patients with driver alterations in MET (mutations and gene amplification) and Axl (rearrangements) that occur in approximately 8% of patients with non-small cell lung cancer (NSCLC). Glesatinib is being evaluated in a Phase 1b study in patients with solid tumors that have genetic alterations in MET or AXL genes. The Phase 2 trial in NSCLC patients with MET genetic alterations is underway to confirm and extend the data that supports the clinical benefit of glesatinib in patients with driver mutations in MET. Genetic alterations in these targets have been implicated as drivers of tumor growth and disease progression in NSCLC, gastroesophageal cancer and other solid tumors. MET and Axl are also implicated as drivers of tumor progression in patients whose tumors have become resistant to EGFR inhibitors. Therefore, Mirati believes that the combination of glesatinib with an EGFR inhibitor could potentially treat patients who have become resistant to agents targeting EGFR. Mirati retains worldwide rights to glesatinib.

**About Mirati Therapeutics**

Mirati Therapeutics develops molecularly targeted, single agent and immuno-oncology combination therapies intended to treat cancer. Mirati’s approach combines the three most important factors in oncology drug development, 1) researching and developing drug candidates that target genetic and epigenetic drivers of cancer, 2) designing creative and agile clinical development strategies that select for patients whose tumors are dependent on specific driver alterations, and 3) leveraging a highly accomplished oncology precision medicine leadership team. The Mirati team uses a blueprint - proven by their prior work - for developing potential breakthrough cancer therapies, with accelerated development paths, in order to improve outcomes for patients. Mirati is advancing three drug candidates through clinical development for multiple oncology indications. More information is available at [www.mirati.com](http://www.mirati.com).

**Forward Looking Statements**

Certain statements contained in this news release, other than statements of fact that are independently verifiable at the date hereof, contain "forward-looking" statements, within the meaning of the Private Securities Litigation Reform Act of 1995, that involve significant risks and uncertainties. For more detailed disclosures and discussions regarding such forward looking statements, please refer to Mirati's filings with the U.S. Securities and Exchange Commission ("SEC"), including without limitation Mirati's filings on Forms 10-K, 10-Q, and 8-K. Forward looking statements are based on the current expectations of management and upon what management believes to be reasonable assumptions based on information currently available to it. Such statements can usually be identified by the use of words such as "may," "would," "believe," "intend," "plan," "anticipate," "estimate," "expect," and other similar terminology, or by statements that certain actions, events or results "may" or "would" be taken, occur or be achieved. Such statements include, but are not limited to, statements regarding Mirati's development plans and timelines, potential regulatory actions, expected use of cash resources, the timing and results of clinical trials, and the potential benefits of and markets for Mirati's product candidates. Forward looking statements involve significant risks and uncertainties and are neither a prediction nor a guarantee that future events or circumstances will occur. Such risks include, but are not limited to, potential delays in development timelines or negative clinical trial results, reliance on third parties for development efforts, changes in the competitive landscape, changes in the standards of care, as well as other risks described in Mirati's filings with the SEC. We are including this cautionary note to make applicable, and to take advantage of, the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 for forward-looking statements. The information in this news release is given as of the date above and Mirati expressly disclaims any obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.


SOURCE Mirati Therapeutics, Inc.