Initial Data from Ongoing Expansion Study of MGCD265 Show Preliminary Evidence of Clinical Efficacy in Heavily Pretreated Non-Small Cell Lung Cancer (NSCLC) Patients with MET Gene Alterations

- The First Three Patients Selected for MET Gene Alterations in MGCD265 Dose Expansion Cohort Show Clear Evidence of Tumor Regression
- MGCD265 is Well Tolerated in Dose Escalation and Dose Expansion Phases
- Data from MGCD265 Phase 1/1b Study Presented at ASCO 2015
- Company Also Provided Updates For Ongoing MGCD516 Dose Escalation Study and Mocetinostat Phase 2 Bladder Cancer Study at the Conference

CHICAGO, May 30, 2015 /PRNewswire/ -- Mirati Therapeutics, Inc. ("Mirati") (NASDAQ: MRTX) today presented data that demonstrated preliminary evidence of clinical activity from its investigational targeted tyrosine kinase inhibitor candidate, MGCD265, as part of the developmental therapeutics category at the 2015 American Society of Clinical Oncology (ASCO) Annual Meeting being held in Chicago from May 29-June 2, 2015. The Company also provided updates on its other targeted tyrosine kinase inhibitor, MGCD516, and spectrum-selective HDAC inhibitor, mocetinostat. Both MGCD516 and mocetinostat were presented as clinical trials in progress at the conference.

"New cancer therapies specifically targeting genetic drivers in selected patients may represent a significant advance compared to traditional chemotherapy," said Christian Kollmannsberger, M.D., British Columbia Cancer Agency, Vancouver Cancer Centre. "MGCD265 is a receptor tyrosine kinase inhibitor that selectively targets tumors in patients with MET or Axl gene alterations. In an ongoing single agent expansion study of MGCD265 in non-small cell lung cancer patients with these alterations, we have seen significant tumor regression in three patients as well as improvement in clinical symptoms such as pain and shortness of breath. Data from this study indicate that MGCD265 can fully inhibit MET and Axl, is well tolerated and should be studied further to define the benefit to patients with lung cancer."

"Data from the Phase 1/1b expansion study presented today clearly demonstrate the anti-tumor activity of MGCD265 and support our hypothesis that targeting MET driver alterations is a clinically valid approach. MGCD265 is the first MET inhibitor targeting MET mutations, MET gene amplification and Axl rearrangements. Collectively, these driver alterations comprise up to 8% of patients with non-small cell lung cancer," said Charles M. Baum, M.D., Ph.D., president and CEO, Mirati. "We are very encouraged by the initial results from this study. The first three non-small cell lung cancer patients with MET exon 14 deletion mutations or MET gene amplification showed clear tumor regression as early as the first assessment and the trial continues to enroll additional patients. Treatment was well tolerated in dose escalation and dose expansion cohorts and PK/PD data demonstrated robust inhibition. These data increase our confidence in the program and we expect to initiate a single arm registration-enabling study in NSCLC by the end of the year."

MGCD265 Phase 1/1b Study, Expansion Cohort:
MGCD265 is an inhibitor of the MET and Axl receptor tyrosine kinase pathways which, when mutated, are drivers of tumor growth. Preclinical data have shown that MGCD265 can potently inhibit tumor cell growth in vitro. Tumor xenograft data demonstrated that tumors with MET exon 14 deletion mutations or MET gene amplification treated with MGCD265 resulted in complete tumor regression, and were predictive of clinical data observed in the ongoing MGCD265 expansion study. This open label, single agent study is designed to evaluate the safety, tolerability, pharmacokinetics/pharmacodynamics (PK/PD) and clinical activity of twice-daily (BID) MGCD265 in patients who have failed at least one prior therapy.

This multinational study began enrollment at the end of December 2014 and continues to enroll NSCLC patients with MET or Axl genetic alterations.

Evidence of clinical activity
Patients receive 1050 mg of MGCD265 BID for 21-day cycles and are assessed for response after every second treatment cycle. At the time of this initial analysis, the first three NSCLC patients with MET gene alterations showed a clinical benefit, including clear tumor regression and improvement in clinical symptoms such as pain and shortness of breath. Currently, these patients do not meet strict criteria for RECIST responses. Patient details are noted below. (The MGCD265 Phase 1/1b study poster presented at ASCO contains additional information, including patient scans noted below, and can be found on the Company's website at www.mirati.com.)
76-year old female: Adenocarcinoma of the lung with a MET exon 14 deletion mutation. The patient enrolled in the study with lung metastases, retroperitoneal and retrocrural lymph nodes and pleural effusion. The patient had undergone platinum-based chemotherapy followed by PD-L1 inhibitor therapy with the best response to each therapy being progressive disease. The first scan after treatment with MGCD265 demonstrated cavitation of the lung/retroperitoneal mass with resolution of pain and cough. The patient continues on the study and is currently in Cycle 5.

70-year old female: History of refractory metastatic adenocarcinoma of the lung with a MET exon 14 deletion mutation. The patient enrolled in the study with extensive liver metastases, right pulmonary lesion and had undergone neoadjuvant chemoradiation, radical pneumonectomy for T3N1 disease, received chemoradiation for pleural and bone metastases, Stereotactic Body Radiation Therapy (SBRT) for pulmonary metastasis, and resection of recurrence in the colon. The first scan after treatment with MGCD265 showed extensive tumor necrosis and regression. The patient continues on the study and is currently in Cycle 6.

51-year old female: Adenocarcinoma of the lung with MET amplification. The patient enrolled in the study with extensive lung disease, bone and brain metastases. The patient had received an EGFR inhibitor, undergone chemotherapy and whole brain radiation. The first scan after treatment with MGCD265 demonstrated regression of tumors in the lung. The patient continues on the study and is currently in Cycle 3.

Safety and tolerability
In the dose escalation phase of the study, the maximum tolerated dose of MGCD265 was 1050 mg BID. This dose was shown to result in > 90% inhibition of MET and Axl based on preclinical predictions and biomarkers sMET and sAxl. The dose limiting toxicities were grade 3 fatigue in one patient and grade 3 diarrhea in one patient. In the dose escalation cohort, MGCD265 was well tolerated at the 1050 mg BID dose and diarrhea in subsequent patients is managed with standard doses of the anti-diarrhea loperamide.

The Company expects to initiate a single arm Phase 2 registration-enabling study in NSCLC by the end of the year.

"While the initial focus of the single agent MGCD265 program is on non-small cell lung cancer, MET is a critical driver in other solid tumors. As approximately five percent of gastric cancer patients have MET gene amplification, gastric cancer represents a significant area for expanded development and, we believe, that MGCD265 could result in clinically meaningful responses in this underserved patient population," said Charles M. Baum, M.D., Ph.D., president and CEO, Mirati. "In addition to the single agent opportunity in NSCLC, there is a strong scientific rationale for the combination of MGCD265 with a third-generation EGFR inhibitor. Recent data have reinforced the hypothesis that MET and Axl may play an important role in resistance to EGFR inhibition. We are exploring our options and plan to start a combination study in patients who are becoming resistant to EGFR inhibition."

The MGCD265 Phase 1/1b study poster presented at ASCO can be found on the Company's website at www.mirati.com. Additional information about this clinical trial of MGCD265 is available at www.clinicaltrials.gov using identifier: NCT00697632.

**Mocetinostat Phase 2 Study in Urothelial Bladder Cancer (UC):**
Mocetinostat is a spectrum-selective histone deacetylase (HDAC) inhibitor. This single arm, single agent Phase 2 clinical trial is designed to evaluate the efficacy, safety, tolerability and PK of mocetinostat as a treatment for a select group of patients with advanced urothelial carcinoma of the bladder.

The primary objective of the study is to determine the clinical activity of mocetinostat in patients with previously treated, locally advanced, unresectable or metastatic urothelial carcinoma of the bladder harboring inactivating mutations or deletions of the histone acetyltransferase genes CREBBP and/or EP300 (estimated to occur in approximately 20% of bladder cancer patients). Secondary objectives include evaluation of safety, secondary efficacy endpoints and PK. Mocetinostat is administered orally three times per week on a 28-day cycle.

The mocetinostat Phase 2 study poster presented at ASCO can be found on the Company's website at www.mirati.com. Additional information about this clinical trial of mocetinostat is available at www.clinicaltrials.gov using identifier: NCT02236195.

**MGCD516 Phase 1 Study in NSCLC:**
MGCD516 is a receptor tyrosine kinase (RTK) inhibitor targeting the RET, DDR and Trk tyrosine kinase signaling pathways, which are reported to be oncogenic drivers. This Phase 1, open label, single agent study is designed to evaluate the safety, PK/PD and clinical activity of MGCD516 in patients with advanced solid tumors, with an initial focus on NSCLC.

The primary objective of the dose escalation phase of the study is to characterize the safety of MGCD516, determine a Phase 2 dose and establish the maximum tolerated dose. MGCD516 is orally administered to unselected patients with advanced solid tumors once daily (QD) on a 21-day cycle. The study is exploring escalating doses of 10 mg, 20 mg, 40 mg, 80 mg and 110 mg to date. Patients have been enrolled across all dosing cohorts and dose escalation will continue until a maximum tolerated dose is established.

The MGCD516 Phase 1 study poster presented at ASCO can be found on the Company's website at www.mirati.com.
Mirati to Present at Jefferies 2015 Global Healthcare Conference

Mirati will also be presenting at the Jefferies 2015 Global Healthcare Conference on Wednesday, June 3 at 8:00 a.m. ET/5:00 a.m. PT in New York. Charles M. Baum, M.D., Ph.D., president and CEO of Mirati, will provide a corporate overview.

A live audio webcast of the presentation will be accessible on the "Investors" page of Mirati's corporate website at www.mirati.com. A replay of the presentation will be available at the same location for 60 days following the conference.

About NSCLC

Despite available treatment options, the overall five year survival rate for patients with NSCLC is only 16.8% 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, and VEGF monoclonal antibodies. 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). MET mutations, including exon 14 deletion mutations, and MET gene amplification each exhibit the key characteristics of driver oncogenes in NSCLC. Rearrangements of the Axl tyrosine kinase gene also appear to be a driver of tumor growth and occur in ~1% of patients with NSCLC.

Extensive preclinical and clinical data indicate that activation of the MET pathway can result in resistance to EGFR inhibitors, as well as the third-generation EGFR inhibitors that are active against tumors with T790 mutations. Resistance is mediated through mutation and/or overexpression of alternative 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. Research has shown that EGFR inhibitor resistance can be reversed in vivo by combined EGFR and MET inhibition, a finding that validates combination therapy with EGFR and MET inhibitors to address therapeutic resistance.

About MGCD265

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). MGCD265 is in the expansion phase of a Phase 1/1b dose escalation study for NSCLC patients with MET or Axl genetic alterations. 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, the combination of MGCD265 with an EGFR inhibitor could treat patients who have become resistant to agents targeting EGFR. Mirati retains worldwide rights to MGCD265.

About Mocetinostat

Mocetinostat is an orally bioavailable, spectrum-selective HDAC inhibitor. Mocetinostat is currently in a Phase 2 trial for the treatment of patients with bladder cancer that carry inactivating mutations of the histone acetyltransferase genes CREBBP and EP300. An investigator-sponsored Phase 2 study evaluating mocetinostat as a treatment for diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL) is underway. The U.S. FDA has granted Orphan Drug Designation to mocetinostat as a treatment for DLBCL. Mirati retains worldwide rights to mocetinostat with the exception of certain Asian territories where the program is partnered with Taiho Pharmaceutical Co., Ltd.

About MGCD516

MGCD516 is a tyrosine kinase inhibitor that has demonstrated potent inhibition of a closely related spectrum of tyrosine kinases, including RET, DDR and Trk, which are key regulators of signaling pathways that lead to cell growth, survival and tumor progression. These kinases and their key regulatory pathways are genetically altered in multiple cancer indications and act as oncogenic drivers that promote cancer development and progression in solid tumors, including NSCLC. MGCD516 is in a Phase 1 dose escalation study in advanced solid tumors with an initial focus on NSCLC. Mirati retains worldwide rights to MGCD516.

About Mirati Therapeutics

Mirati Therapeutics develops molecularly targeted cancer treatments that are intended to inhibit tumor growth. 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 targeted oncology 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 standard 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.

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