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Onconova Advances Oral Rigosertib to Phase II Clinical Trial in Myelodysplastic Syndromes

Complete Phase I Data to be Reported at ASCO 2012 Annual Meeting

MAY 10, 2012 – NEWTOWN, PA & PENNINGTON, NJ: Onconova Therapeutics, Inc., announced today the advancement of the oral formulation of rigosertib (Estybon®, ON 01910.Na), an anticancer agent with demonstrated activity in solid tumors and hematologic malignancies, into a new Phase II study. The intravenous (IV) formulation of rigosertib is currently in a pivotal Phase III trial for refractory myelodysplastic syndromes (MDS) in the U.S. and EU.

“A randomized Phase II evaluation of oral rigosertib will be conducted in patients with Low or Intermediate-1 risk transfusion-dependent myelodysplastic syndromes at Columbia University Medical Center,” said Siddhartha Mukherjee, MD, DPhil, Principal Investigator of the study, Assistant Professor of Medicine at Columbia University and staff physician at Herbert Irving Comprehensive Cancer Center of Columbia University Medical Center/New York-Presbyterian Hospital in New York. “This is a significant step forward in the development of this new medicine. The objective of the study is to determine if oral rigosertib will reduce the need for blood transfusions in transfusion-dependent MDS patients. The need for blood transfusions and the complications from receiving transfusions are serious medical issues for these patients."

This Phase II study follows the positive findings of a Phase I dose escalation study in MDS patients treated with orally-administered rigosertib. These findings were presented at the December 2011 American Society of Hematology Annual Meeting (Blood 118: Abstract 3797, 2011).

- In the Phase I study, orally delivered rigosertib was well tolerated and bioavailable. Clinical activity observed included favorable bone marrow responses in high-risk patients who were refractory to hypomethylating agents, a reduction in need for red blood cell (RBC) transfusions in transfusion-dependent patients, and a transition to transfusion independence. Rami Komrokji, M.D. and colleagues, and Azra Raza, M.D., conducted the trial at the H. Lee Moffitt Cancer Center and Columbia University Medical Center, respectively.

The final analysis of the Phase I clinical trial, along with results from a separate study of oral rigosertib in patients with solid tumors, will be reported in two presentations at the 2012 American Society of Clinical Oncology (ASCO) Annual Meeting, in Chicago, June 1-5.

“The reduction in RBC transfusions observed in this study was a breakthrough,” said Dr. Raza. “Confirmation of these findings in the Phase II study will be a significant step forward, potentially leading to a safe and effective treatment for patients with low-risk MDS.”

About ONTIME
ONTIME (ON 01910.Na Trial In MyelodysplasticSyndromE) is a pivotal Phase III, multicenter, randomized trial, comparing rigosertib plus best supportive care to best supportive care alone, in high-risk MDS patients with excess blasts (5% to 30% bone marrow blasts), who are refractory, intolerant to, or have relapsed after azacitidine or decitabine treatment. ONTIME is enrolling patients in the United States and five countries in the EU. Additional information about this trial is available at www.clinicaltrials.gov.

About Rigosertib
Rigosertib (Estybon®, ON 01910.Na) is a small molecule inhibitor of critical pathways important in the growth and survival of cancer cells. Extensive Phase I and Phase II studies with rigosertib have been conducted at leading institutions in the U.S. and abroad in more than 500 patients with solid tumors and hematological cancers, including MDS and AML. Based on data from clinical studies that explored various doses and regimens of intravenous rigosertib, the most common adverse events that were reported in 20-35% of patients were: fatigue, abdominal cramping, pain, nausea, gas, vomiting, and diarrhea. MDS and AML are blood disorders widely recognized as difficult to manage, with limited therapeutic options available for patients, especially those with drug-resistant disease. The multi-site Phase III ONTIME (ClinicalTrials.gov identifier, NCT01241500) trial in MDS patients is being conducted under a Special Protocol Assessment (SPA) from the U.S. Food and Drug Administration (FDA) and is being supported by an award from the Therapeutics Acceleration Program (TAP) of The Leukemia and Lymphoma Society (LLS). Both the FDA and European Medicines Agency have granted Orphan Drug Designation for the use of rigosertib in MDS. The rigosertib clinical program in solid tumors is also advancing. In a Phase II/III adaptive design trial, ONTRAC (ON 01910.Na TRial in Patients with Advanced Pancreatic Cancer) is a Phase II/III, multicenter, randomized, controlled study to compare the efficacy and safety of gemcitabine alone vs. rigosertib combined with gemcitabine in patients with previously untreated metastatic pancreatic cancer (ClinicalTrials.gov identifier, NCT01360853).

About Myelodysplastic Syndromes
Myelodysplastic Syndromes (MDS) is a heterogeneous group of clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis (blood cell production) involving one or more cell lineages (red blood cells, white blood cells or platelets) and a viable risk of transformation to acute myeloid leukemia. It is estimated that MDS affects more than 300,000 people worldwide. In June 2010 the Journal of Clinical Oncology[1] published a study by Goldberg et al. demonstrating 45,000 new cases of MDS are diagnosed each year in the United States. MDS patients often require multiple blood transfusions and extensive supportive care to manage their disease. While MDS can occur in people of all ages, it is diagnosed most frequently in adults over 60 years of age.

About Onconova Therapeutics, Inc.
Onconova Therapeutics based in Newtown, PA and Pennington, NJ, discovers and develops novel small molecule therapeutics directed against targets involved in signal transduction, cellcycle, and DNA repair. In addition to rigosertib, Onconova is developing two other clinical trialstage products: ON 01210.Na (Ex-RAD®), a radioprotectant, and ON 013105, a novel anticancer agent initially directed to refractory lymphoma, including Mantle Cell Lymphoma. For additional information, please visit http://www.onconova.com.

[1] - Journal of Clinical Oncology, June 10, 2010; Volume 28, Number 17, *J Clin Oncol 28:2847-2852*, Incidence and Clinical Complications of Myelodysplastic Syndromes Among United States Medicare Beneficiaries

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