February 2, 2015

Onconova Announces Clinical Development Plan for Rigosertib in Higher Risk Myelodysplastic Syndrome (HR-MDS) Patients After Failure of Treatment With Hypomethylating Agents (HMAs)

- Clarity of the design of Phase 3 global replication trial of IV rigosertib in HR-MDS
- Updates on development programs for oral rigosertib as a single agent and in combination with azacitidine; additional data expected for both in 2015

NEWTOWN, Pa., Feb. 2, 2015 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (Nasdaq:ONTX) a clinical-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer, today announced that following discussions regarding the future development of rigosertib with the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and several European national regulatory agencies, the Company has solidified its plans for a Phase 3 clinical trial for rigosertib in HR-MDS patients after failure of treatment with HMAs. Pending regulatory approvals and appropriate financing, Onconova hopes to initiate trial enrollment during the second half of 2015.

In February 2014, Onconova announced top-line results of its ONTIME trial, a Phase 3 clinical trial of an intravenous formulation of rigosertib, or rigosertib IV, in patients with HR-MDS. The ONTIME trial did not meet its primary endpoint in the intent-to-treat population, but improvements in median overall survival (mOS) were observed in various pre-specified and exploratory subgroups of patients, including "primary HMA failure" patients (those who had progressed on or failed to respond to previous treatment with HMAs) and patients in the Revised International Prognostic Scoring System (IPSS-R) Very High Risk category (IPSS-R calculates a risk score for MDS patients based on the location and type of chromosome abnormalities, number and degree of cytopenias, and percentage of bone marrow blasts observed at diagnosis). Among the 184 patients (62% of patients in the trial) with primary HMA failure, mOS was 8.6 months in the rigosertib arm (127 patients) compared to 5.3 months in the best supportive care arm (57 patients), with a hazard ratio of 0.69 and a p value of 0.040. Among the 134 patients (45% of patients in the trial) who were in the IPSS-R Very High Risk category, mOS was 7.6 months in the rigosertib arm (93 patients) compared to 3.2 months in the best supportive care arm (41 patients), with a hazard ratio of 0.56 and a p value of 0.005. Further, the safety and tolerability of rigosertib IV in the ONTIME trial was acceptable.

Based on subgroup analyses and the current lack of any approved second-line therapies for HR-MDS patients, Onconova explored various approval pathways with the regulatory agencies. An unmet medical need exists for MDS patients who do not benefit from HMA therapies. The potential for refining the clinical indication was discussed with both the FDA and EMA, based on the demonstration of heterogeneity in the ONTIME trial patient population and the consequent definition of subgroups with high prognostic risk that appear to derive a greater benefit from rigosertib treatment. Both the FDA and EMA have expressed a preference for a randomized controlled trial with overall survival and overall response as clinically meaningful endpoints. Therefore, based on the feedback from the FDA and the EMA, and utilizing the results of the ONTIME trial, a randomized controlled trial in a more homogeneous patient population is being developed for regulatory review.

"We are encouraged by our analyses of rigosertib ONTIME trial results in primary HMA failure patients and IPSS-R Very High Risk patients," said Ramesh Kumar, Ph.D., President and CEO of Onconova. "There have been no drug approvals in the U.S. since 2005 to address the unmet medical need of these patients. We remain committed to developing rigosertib IV to meet the needs of this underserved patient population. With regulatory guidance from both the FDA and the EMA, we will work expeditiously to finalize the design for, and initiate, the required pivotal trial."

Oral rigosertib for lower risk MDS (LR-MDS)

Onconova was notified that Baxter Healthcare SA, Onconova's commercialization partner in Europe, has elected not to pursue additional clinical trials, or the submission of a drug approval application, for rigosertib oral in LR-MDS patients. Onconova would have received a milestone payment under its agreement with Baxter if the parties had mutually agreed to progress the development of oral rigosertib in LR-MDS patients. The decision by Baxter does not alter the collaboration agreement between the parties, and Onconova has the right to continue the development of oral rigosertib in this indication on its own. Onconova is enrolling LR-MDS patients in an extended portion of a Phase 2 clinical trial to assess the utility of bone marrow methylation patterns and genomic DNA testing for the identification of patients more likely to respond to rigosertib. Onconova expects to make a determination regarding the future clinical development strategy for oral rigosertib in LR-MDS employing a predictive biomarker approach after data from these studies become available.

Oral rigosertib in combination with azacitidine for MDS and AML

Onconova continues to advance the development of oral rigosertib in combination with azacitidine for the treatment of front-line

and second-line MDS and AML patients. The Phase 2 portion of an ongoing clinical trial has been designed to assess whether treatment with rigosertib, in combination with azacitidine, has a beneficial effect on bone marrow and peripheral blood blast cell counts, and bone marrow function in patients with MDS and AML. Patient enrollment in this Phase 2 trial is projected to be completed by the end of the second quarter of this year. Additional Phase 2 data are expected to be presented at a scientific conference in the second quarter of 2015.

About Rigosertib

Rigosertib is a small molecule that inhibits cellular signaling by acting as a Ras mimetic. This is believed to be mediated by direct binding of rigosertib to the Ras-binding domain (RBD) found in many Ras effector proteins, including the Raf kinases and PI3K. The initial therapeutic focus for rigosertib is myelodysplastic syndromes (MDS), a group of bone marrow disorders characterized by ineffective formation of blood cells that often converts into acute myeloid leukemia (AML). Clinical trials with intravenous (IV) and oral formulations of rigosertib are being conducted at leading institutions in the U.S. and abroad. To date, more than 500 MDS patients have been enrolled in clinical trials with rigosertib. Rigosertib is covered under composition of matter patents issued worldwide. Orphan designation has been granted for rigosertib in MDS in the U.S., Europe, Australia and Japan.

About Onconova Therapeutics, Inc.

Onconova Therapeutics is a clinical-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer. Onconova's clinical and pre-clinical stage drug development candidates are derived from its extensive chemical library and are designed to work against specific cellular pathways that are important in cancer cells, while causing minimal damage to normal cells. In addition to rigosertib, the Company's most advanced product candidate, two other candidates are clinical stage, and several candidates are in pre-clinical stages. For more information, please visit http://www.onconova.com.

Forward Looking Statements

Some of the statements in this release are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995, which involve risks and uncertainties. These statements relate to future events or Onconova Therapeutics, Inc.'s future operations, clinical development of Onconova's product candidates and presentation of data with respect thereto, regulatory approvals, expectations regarding the sufficiency of Onconova's cash and other resources to fund operating expenses and capital expenditures, Onconova's anticipated milestones and future expectations and plans and prospects. Although Onconova believes that the expectations reflected in such forward-looking statements are reasonable as of the date made, expectations may prove to have been materially different from the results expressed or implied by such forward-looking statements. Onconova has attempted to identify forward-looking statements by terminology including "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately" or other words that convey uncertainty of future events or outcomes. These statements are only predictions and involve known and unknown risks, uncertainties, and other factors, including those discussed under the heading "Risk Factors" in our most recent Annual Report on Form 10-K and quarterly reports on Form 10-Q.

Any forward-looking statements contained in this release speak only as of its date. We undertake no obligation to update any forward-looking statements contained in this release to reflect events or circumstances occurring after its date or to reflect the occurrence of unanticipated events.

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