Onconova Presents Promising Data from Phase 2 Expansion Study of Oral Rigosertib and Azacitidine Combination in Patients with Myelodysplastic Syndromes at 6th International Bone Marrow Failure Disease Symposium

March 26, 2018

- First presentation from dose exploration cohorts in an expanded trial addressing urinary safety of the novel combination therapy in higher risk patients with Myelodysplastic Syndromes (MDS)
- Study demonstrates elimination of grade 3 or grade 4 urinary adverse events after implementation of mitigation strategies

NEWTOWN, Pa., March 26, 2018 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (NASDAQ:ONTX), a Phase 3 clinical-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer, presented promising new clinical safety data from the expansion phase of a Phase 2 clinical trial at the Bone Marrow Failure Disease Scientific Symposium, held in Rockville, Maryland, on March 22-23, 2018.

Oral rigosertib has been developed as a single agent and in combination with azacitidine. Previous studies have demonstrated that Low-Risk (LR) MDS patients with intermittent oral rigosertib treatment at a dose of 560 mg BID show a transfusion independence rate (TI), as defined by the IWG 2006 criteria, of 44% (Raza, et al, Blood 2017 130:1689). Oral rigosertib in combination with AZA is being studied in patients with Higher-risk (HR) MDS. Initial results of the Phase 2 study with oral rigosertib (840 mg /day 3 out of 4 weeks) in combination with azacitidine in patients with MDS demonstrated an overall response rate of 76%; 62% in patients following hypomethylating agent (HMA) failure; and 85% in HMA naïve patients (Navada *et al*, EHA, 2017). In both single agent and combination studies, oral rigosertib has been associated with hematuria in a subset of patients which has been shown to be dose and administration scheme dependent (Garcia-Manero G, Blood 2016 128:2011). The results reported here are from a dose exploration study in HR MDS patients with an increased oral rigosertib dose (1120 mg/day 3 out of 4 weeks) and focus on the impact of risk-mitigation strategies in minimizing the incidence of urinary adverse events (UAEs); including hematuria. The mitigation strategies included prescribing the second dose of rigosertib earlier in the day and encouraging bladder emptying at bedtime.

The reported incidence of hematuria of any grade with single agent azacitidine is 6.3%, including 2.3% grade 3 and 4 events (per product insert). In the combination trial of oral rigosertib (total dose of 840 mg/day 3 out of 4 weeks) and azacitidine, the incidence of hematuria was 48%, with grade 3 or grade4 AEs of 12%. In the new study, in 37 patients studied with oral rigosertib (total dose of 1120 mg/day 3 out of 4 weeks) and azacitidine employing prophylactic risk-mitigating strategies to minimize hematuria, a significantly lower incidence of grade 1 & 2 hematuria (11%), and no grade 3 or 4 hematuria have been seen to date.

Guillermo Garcia-Manero, M.D, Professor and Chief of the MDS Section at the MD Anderson Cancer Center, who presented the new results, commented, “Choices are very limited for higher risk MDS, with two HMAs as the only drugs approved by the Health Authorities for these patients. There is an urgent need to develop novel approaches, including combination therapies that can improve the outcomes in patients who require an HMA. The previously presented studies of the combination regimen of oral rigosertib with azacitidine have demonstrated impressive evidence of efficacy in HMA naïve and HMA refractory patients with higher-risk MDS. Since the success of a combination therapy is greatly influenced by the safety and tolerability of the regimen, the new results of improved tolerability are of great importance for the proposed pivotal study of this combination. The ability to ensure longer duration of treatment without interruption or dose reduction due to an acceptable safety profile can ensure optimal benefit for patients. We look forward to participating in the planned Phase 3 study of this novel approach, which combines two agents with distinct mechanisms of action for the potential benefit of frontline MDS patients.”

Dose optimization and risk mitigation strategies undertaken specifically to minimize UAEs associated with oral rigosertib in combination with azacitidine have resulted, to date, in a decrease in frequency of hematuria from 48% to 11% and elimination of any serious grade 3 events. Minimization of AEs permits patients to continue on treatment to optimize the potential benefit. Reduction in incidence of hematuria also enables the continued study of oral rigosertib in LR-MDS, based on the promising TI Rate previously reported.

A copy of the poster is available by visiting the Scientific Presentations section of Onconova’s website.

About Onconova Therapeutics, Inc.

Onconova Therapeutics, Inc. is a Phase 3-stage biopharmaceutical company focused on discovering and developing novel small molecule drug candidates to treat cancer, with a primary focus on Myelodysplastic Syndromes (MDS). Rigosertib, Onconova's lead candidate, is a proprietary Phase 3 small molecule agent, which Onconova believes blocks cellular signaling by targeting RAS effector pathways. Using a proprietary chemistry platform, Onconova has created a pipeline of targeted agents designed to work against specific cellular pathways that are important in cancer cells. Onconova has three product candidates in the clinical stage and several pre-clinical programs. Advanced clinical trials with the Company’s lead compound, rigosertib, are aimed at what the Company believes are unmet medical needs of patients with MDS. For more information, please visit http://www.onconova.com.

About IV Rigosertib

The intravenous form of rigosertib has been employed in Phase 1, 2, and 3 clinical trials involving more than 800 patients, and is currently being evaluated in a randomized Phase 3 international INSPIRE trial for patients with higher-risk MDS, after failure of hypomethylating agent, or HMA,

therapy.

About INSPIRE

The **IN**ternational **S**tudy of **P**hase III **I**V **R**igos**E**rtib, or INSPIRE, was finalized following guidance received from the U.S. Food and Drug Administration and European Medicines Agency and derives from the findings of the ONTIME Phase 3 trial. INSPIRE is a multi-center, randomized controlled study to assess the efficacy and safety of IV rigosertib in HR-MDS patients who had progressed on, failed to respond to, or relapsed after previous treatment with an HMA within the first 9 months or nine cycles over the course of one year after initiation of HMA treatment. This time frame optimizes the opportunity to respond to treatment with an HMA prior to declaring treatment failure, as per NCCN Guidelines. Following interim analysis in early 2018, the independent Data Monitoring Committee recommended that the trial continue with an expansion in enrollment to 360 patients based on a pre-planned sample size re-estimation. Patients are randomized at a 2:1 ratio into two treatment arms: IV rigosertib plus Best Supportive Care versus Physician's Choice plus Best Supportive Care. The primary endpoint of INSPIRE is overall survival. Full details of the INSPIRE trial, such as inclusion and exclusion criteria, as well as secondary endpoints, can be found on clinicaltrials.gov (NCT02562443).

About Oral Rigosertib

The oral form of rigosertib was developed to provide more convenient dosing for use where the duration of treatment may extend to multiple years. This dosage form may also support many combination therapy modalities. To date, 368 patients have been treated with the oral formulation of rigosertib. Initial studies with single-agent oral rigosertib were conducted in hematological malignancies, lower-risk MDS, and solid tumors. Combination therapy of oral rigosertib with azacitidine and chemoradiotherapy has also been explored. Currently, oral rigosertib is being developed as a combination therapy together with azacitidine for patients with higher-risk MDS who require HMA therapy. A Phase 1/2 trial of the combination therapy has been fully enrolled and the preliminary results were presented in 2016. This novel combination is the subject of an issued US patent with earliest expiration in 2028.

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, and involve risks and uncertainties. These statements relate to Onconova Therapeutics, Inc.'s expectations regarding the INSPIRE Trial. 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 Onconova's ability to continue as a going concern, the need for additional financing and current plans and future needs to scale back operations if adequate financing is not obtained, the success and timing of Onconova's clinical trials and regulatory approval of protocols, and those discussed under the heading "Risk Factors" in Onconova's 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. Onconova undertakes 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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