Onconova Highlights Results from Phase 2 Trial of Oral Rigosertib In Combination with Azacitidine (Vidaza®) in Myelodysplastic Syndromes (MDS) at the 2018 ASH Annual Meeting

December 3, 2018

- Overall response rate (ORR) of 90% reported in this multi-institutional Phase 2 study in hypomethylating agent (HMA) naïve patients, including Complete Remission (CR) rate of 34%
  - ORR of 54% and CR/Partial Response (PR) of 8% in HMA failed patients
- Median duration of response for the HMA naïve patients was 12.2 months
  - Median duration of response for the HMA failed patients was 10.8 months
- Based on the safety and efficacy profile of this novel combination, a pivotal Phase 3 trial is planned in an HMA and chemotherapy naïve Higher Risk (HR)- MDS patient population

NEWTOWN, Pa., Dec. 03, 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, announces the presentation of the efficacy and safety results of oral rigosertib in combination with azacitidine (Vidaza®) in patients with HR-MDS reported at an oral presentation during the 60th American Society of Hematology (ASH) Annual Meeting and Exposition in San Diego. Rigosertib, the Company's lead compound, is being evaluated in both intravenous and oral forms.

ORAL PRESENTATION:

Phase 2 Expansion Study of Oral Rigosertib Combined with Azacitidine treatment in Patients with Higher-Risk (HR) Myelodysplastic Syndromes (MDS): Efficacy and Safety Results in HMA Treatment Naïve & Relapsed (Rel)/Refractory (Ref) Patients

Session Name: 637. Myelodysplastic Syndromes – Clinical Studies: Novel Therapeutics I
Date: Saturday, December 1, 2018
Presentation Time: 4:15 PM PST

Seventy-four (74) patients were treated with a median age of 69 years (range 42-90) at 9 clinical sites, and received either 840 mg or 1,120 mg of oral rigosertib daily divided into two doses, in combination with a standard dose of injectable azacitidine. Of the 55 evaluable patients, 29 patients were treated with a daily dose of 1,120 mg of oral rigosertib, either 560 mg twice daily (12 patients) or 840 mg in the a.m. and 280 mg in the afternoon (17 patients). Twenty-six patients were treated with 560 mg in the AM and 280 mg in the PM (daily dose of 840 mg) for the first three weeks of a four-week cycle. All patients also received 75 mg/m^2/day SC or IV azacitidine during the second week of the four-week cycle. The median duration of treatment for the HMA naïve and HMA failed patients was 7.8 and 4.9 months respectively. The median duration of response in these groups was 12.2 and 10.8 months, respectively.

The overall response rate (ORR) using the IWG 2006 criteria, in 29 HMA naïve patients, was 90%; including 10 patients (34%) with Complete Remission (CR). Among the 26 evaluable HMA-failed patients the ORR was 54% including 8% CR or PR. The median time to initial and best response were 1 and 4 cycles in the HMA naïve group and 2 and 5 cycles in the HMA failed group.

The safety population (n = 74) received at least 1 dose of oral rigosertib. The combination was well tolerated. Other than genitourinary adverse events (AEs), the AE profile was similar to those described for azacitidine alone in this patient population. Genitourinary AEs, including hematuria (45% incidence of all grades, including 9% grade 3, and dysuria (38% all grades and 9% grade 3) were observed. A Safety Optimization Strategy was implemented for the higher dose cohort of 1,120 mg of oral rigosertib. These strategies included earlier in the day administration of the PM dose, oral hydration, monitoring of urinary pH and mandatory bladder emptying at night. Collectively these strategies resulted in mitigation of the target genitourinary AEs, including reduction of genitourinary grade 3 AEs reported from an earlier cohort despite receiving a higher dose of oral rigosertib.

In conclusion, oral rigosertib in combination with azacitidine was well tolerated in HMA naïve and HMA failed HR-MDS patients. The combination produced an encouraging rate of overall response and complete remission in both groups. The safety optimization strategies and increased dose exploration of oral rigosertib in the combination is leading to the development of a pivotal Phase 3 trial in HMA and chemotherapy naïve patients.

Drs. Lewis Silverman and Guillermo Garcia Manero, the lead investigators of the study at Mount Sinai Medical Center and MD Anderson Cancer Center, respectively, commented, "This multi-institutional collaborative study based on earlier laboratory research showing synergistic activity of rigosertib in combination with azacitidine led to a clinical trial of this combination in higher-risk MDS patients for both HMA naive and failed patients. The high overall response rate reported today is impressive, as is the durability and rate of achieving complete remission. We are excited about progressing these studies to a randomized pivotal placebo-controlled Phase 3 trial. The overall tolerability of the combination and convenience of administration of oral rigosertib could be key advantages for these future studies."

Dr. Steve Fruchtman, President of Onconova Therapeutics, Inc, sponsor of this study and developer of rigosertib commented, "We are most grateful to the patients, their families and our dedicated collaborating investigators for their participation in this study. The impressive results presented here have led to our plan for a pivotal trial for these patients ultimately hoping to improve upon their current therapeutic options. Based on End of Phase 2 Meetings with the Health Authorities, we have developed a randomized controlled pivotal trial. We expect to start the regulatory process for the

approval of this trial plan very shortly. We are hopeful that both intravenous and oral formulations of rigosertib will be useful in serving the needs of higher risk MDS patients."

This oral presentation was delivered by Shyamala Navada, MD, Mount Sinai Medical Center on Saturday, December 1, 2018.

A copy of the presentation is available by visiting the Scientific Presentations section of Onconova's website.

Onconova plans to meet with the FDA to discuss the results of the Phase 2 trial and the planned Phase 3 trial, and to seek a Special Protocol Assessment. The Company has partnered rigosertib with SymBio Pharmaceuticals, for Japan and Korea, and with Pint Pharma for Latin American countries. Both partners have indicated their interest in participating in the proposed new pivotal Phase 3 trial by enrolling patients in their respective territories. SymBio is currently conducting Phase 1 studies with oral rigosertib in Japan and also participating in the Phase 3 global INSPIRE trial. The Company is also actively seeking additional collaborations for rigosertib in other geographies.

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 is reported to block 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. 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 9 cycles over the course of one year after initiation and with progression or failure to respond to 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 where the duration of treatment may extend for years in lower risk MDS patients. 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 U.S. 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 expectations regarding the INSPIRE Trial and Onconova's other development plans. 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. 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. 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, 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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