Onconova Presents Data on Rigosertib in Myelodysplastic Syndromes (MDS) at the ASH 2017 Meeting

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- Oral rigosertib as a single agent demonstrates activity in a Phase 2 trial for lower-risk MDS
- 32% of 62 evaluable patients, and 44% of patients receiving optimal dosing, achieved transfusion independence
- New data on the molecular basis of the combination therapy with rigosertib and azacitidine in epigenetic studies in patient derived stem cells

NEWTOWN, Pa., Dec. 12, 2017 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (NASDAQ:ONTX), a Phase 3 clinical-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer, delivered two poster presentations highlighting drug activity and the mechanism of action of rigosertib in Myelodysplastic Syndromes during the 59th American Society of Hematology (ASH) Annual Meeting and Exposition in Atlanta. Rigosertib, the Company's lead compound, is being evaluated in Phase 3 and Phase 2 clinical trials in both intravenous and oral forms, respectively.

Rigosertib Oral is Active as a Single Agent in Lower-risk Transfusion Dependent MDS

Title: *Rigosertib Oral in Transfusion Dependent Lower-Risk Myelodysplastic Syndromes (LR-MDS): Optimization of Dose and Rate of Transfusion Independence (TI) or Transfusion Reduction (TR) in a Single-Arm Phase 2 Study*

Eighty-two patients with a median age of 70 years (range 54-90) were enrolled at 5 clinical sites, and received a median of 5.4 months (range 0.1-28.8) of oral rigosertib. Of the 82 enrolled patients, 9 patients were treated with 560 mg BID continuously, 7 patients were treated with 560 mg in the AM and 280 mg in the PM continuously, 35 patients were treated with 560mg BID intermittently (as defined as 2 out of 3 weeks), and 31 patients were treated with 560mg in the AM and 280mg in the PM intermittently. Sixty patients were treated with ESA and oral rigosertib during the study.

Of the 82 patients, 66 patients received intermittent dosing for at least 8 consecutive weeks; and 20 of 62 evaluable patients (32%) achieved TI lasting 8 to 85+ weeks; with a median of 18 weeks. The highest rate of TI (44%) was observed in the 560 mg BID intermittent cohort: 15 of 34 eligible patients achieved TI lasting 8 to 85+ weeks; with a median of 18 weeks. Ninety-three percent (93%) of these 15 patients received rigosertib with continued ESA.

The safety assessable population (n = 82) received at least 1 week of rigosertib treatment. Notably, no significant treatment emergent myelosuppression, or other notable adverse events (AEs), were evident in these patients. Continuous rigosertib dosing cohorts were closed early due to higher urinary AEs. For all intermittent patients (n=66), the most frequent treatment emergent AEs observed were urinary with pollakiuria (42.4%), fatigue and micturition urgency (33.3%), urinary tract pain (28.8%), hematuria and dysuria (24.2%). Intermittent and reduced dosing of rigosertib (560 mg AM, 280 mg PM during 14 days of 21-day cycles) was associated with a significantly reduced incidence of urinary toxicity. All AEs were reversible once rigosertib dosing was reduced or discontinued. Strategies to ameliorate or manage the urinary AEs are under investigation.

In conclusion, oral rigosertib treatment resulted in high rates of transfusion reduction and TI. Patients administered rigosertib for 2 out of 3 weeks at a dose of 560 mg BID (1120 mg over 24 hours) achieved an impressive TI rate of 44% (15/34). Based on the rate of TI, and the observed urinary AEs, the risk benefit profile of oral intermittent dosing is favorable. Oral rigosertib at a total dose of 1120 mg over 24 hours administered intermittently in HR-MDS patients in combination with azacitidine is now being studied, with further exploration to optimize dose and mitigate urinary AEs.

Dr. Azra Raza, lead investigator of the study, commented, "This collaborative study originated at our clinic in Columbia and spanned several years of treatment and follow-up of transfusion dependent lower-risk MDS patients treated with oral rigosertib. The very high response rate reported is remarkable, as is the noted durable benefit to patients who are burdened by the need for frequent transfusions. Since these patients have few FDA approved therapeutic options, we are excited about expanding these studies to pivotal trials. The tolerability and convenience of administration of oral rigosertib will be key determinants of success in future studies."

This poster presentation was delivered by lead co-author Aref Al-Kali, MD, Division of Hematology, Mayo Clinic, Rochester, MN on Saturday, December 9, 2017. The reported results updated a study lead by Azra Raza, MD, Department of Medicine, Columbia University Medical Center, New York, NY.

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

Mechanistic Rationale of Combination Therapy with Rigosertib

Title: *Effects of Rigosertib (RIGO) Alone or in Combination with Azacitidine or Vorinostat on Epigenetic Reprogramming of CD34+ Cells in the Myelodysplastic Syndrome*

This presentation reported the findings of rigosertib alone or in combination with azacitidine or vorinostat on epigenetic reprogramming or molecular changes of CD34+ cells in MDS. The study results indicate that epigenetic effects of rigosertib on chromatin alterations may lead to improved hematopoietic function and response in the clinical setting, and expanded the understanding of the mechanism of action of rigosertib in combination

with azacitidine. These preclinical models suggest potential novel clinical strategies with rigosertib and azacitidine to improve outcomes for patients with higher-risk MDS. Oral rigosertib in combination with azacitidine is now being studied in higher-risk MDS patients.

Dr. Lewis Silverman, the lead investigator of the study, commented, “A large body of evidence with both intravenous and oral rigosertib supports the activity of this novel agent in MDS patients. Based on our laboratory studies and a US patent, a combination regimen of oral rigosertib with azacitidine has been explored in Phase 2 trials and the promising results of these trials are providing the basis for the design of a pivotal Phase 3 study. Our research continues to explore the mechanistic basis of the impressive and durable responses noted in higher-risk MDS patients at Mount Sinai and other collaborating institutions. Such understanding may permit design of other combinations, as well as biomarkers for patient selection and theranostic uses in the near future.”

This poster presentation was delivered by lead author Lewis R Silverman, MD, Tisch Cancer Institute, Icahn School of Medicine, New York, NY on Monday, December 11, 2017.

A copy of the presentation 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 the Company 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. The advanced clinical trial with the Company’s lead compound, rigosertib, is 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 the randomized Phase 3 international INSPIRE trial for patients with higher-risk (HR) 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, trial design 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 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 the National Comprehensive Cancer Network (NCCN) Guidelines. The trial will enroll approximately 225 patients 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 and an interim analysis is anticipated. 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 also supports 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 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 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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