June 26, 2017

Onconova Therapeutics Presents Rigosertib Data at the 22nd Congress of the European Hematology Association in Madrid

- ***Oral Rigosertib combined with Azacitidine administered to patients with treatment naïve and refractory Acute Myeloid Leukemia and Myelodysplastic Syndromes, demonstrates responses in difficult-to-treat population***
  - ***The combination may overcome hypomethylating agent resistance; further study in Acute Myeloid Leukemia is warranted***
- ***Nonclinical study of Rigosertib combined with Azacitidine suggests epigenetic reprogramming of hematopoietic stem cell populations in patients with Myelodysplastic Syndromes***
- ***Oral Rigosertib as a single agent is well-tolerated in Japanese patients with recurrent/relapsed or refractory Myelodysplastic Syndromes***

NEWTOWN, Pa., June 26, 2017 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (NASDAQ:ONTX), 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), has announced data demonstrating responses of oral rigosertib with azacitidine in Acute Myeloid Leukemia (AML) and Myelodysplastic Syndromes (MDS), as well as oral rigosertib as a single agent. The findings were presented by Onconova, Mount Sinai, and SymBio at the 22nd Congress of the European Hematology Association taking place on June 22-24 in Madrid, Spain.

"Advancing oral rigosertib in the clinic as a stand-alone agent, and providing further evidence for activity of rigosertib in combination with azacitidine in patients with MDS and AML represents an extension of our pipeline," said Dr. Ramesh Kumar, CEO of Onconova. "We are positioned for multiple key milestones in 2017 and beyond, beginning with the interim analysis of our pivotal Phase 3 INSPIRE trial later this year."

Full copies of the posters and oral presentations can be accessed by visiting "Scientific Presentations" in the Investors section of Onconova's website.

Oral Presentation: Oral Rigosertib Combined with Azacitidine in Patients with AML and MDS; Effects in Treatment Naive and Relapsed/Refractory Patients

A novel combination therapy of oral rigosertib plus injectable azacitidine was tested in this trial (09-08) at three sites in the U.S. and Europe, representing a first-in-man study of this approach. Eight AML patients were evaluable for response, with an overall response rate (ORR) of 37.5%, and responses in both secondary and refractory AML. Two additional patients had stable disease (25%). Responses were durable, with the longest response in AML approaching one year.

Among 33 evaluable MDS patients, ORR was 76%. Complete remission (CR) in eight (24%), concurrent marrow CR (mCR) and hematologic improvement (HI) in 10 (30%), mCR alone in six (18%), and HI alone in 1 (3%). ORR was 85% in hypomethylating agent (HMA) naïve patients and 62% in HMA resistant patients.

Earlier, Phase 1 and Phase 2 data in first and second-line higher risk (HR)-MDS patients were presented at the 2016 American Society of Hematology (ASH) Meeting and updated at the 2017 ASH and MDS Foundation meetings. Based on these results, the authors determined that continued study in AML is warranted.

A Phase 3 study of the combination of oral rigosertib and azacitidine in patients with treatment naïve HR-MDS is currently being designed based on an end-of-phase 2 meeting with the Food and Drug Administration.

E-Poster: Rigosertib Combined with Azacitidine Epigenetically Modulates Chromatin and Hematopoietic Stem Cell Populations in MDS

Onconova's collaborators from the Mount Sinai School of Medicine investigated the in vitro effects of rigosertib combined with azacitidine or vorinostat on two cell lines and on bone marrow samples from patients treated in the Phase 1-2 study, obtained prior to and after one cycle of the combination regimen. Azacitidine is an HMA and vorinostat is an inhibitor of Histone Deacetylase. Rigosertib's mechanism of action is reported to be mediated by binding to a Ras Binding Domain present in Ras and its effector proteins, including PI3 Kinase and Raf. Chromatin remodeling by changes in methylation and acetylation were noted in cell-lines treated with all three agents, as well as after treatment with the two combinations. The

nature of the changes induced with the two combinations was distinct.

The authors propose that rigosertib potentially functions as a chromatin modifying agent in combination with azacitidine and may overcome HMA resistance through chromatin remodeling. Rigosertib alone, and in combination, also leads to epigenetic reprogramming of hematopoietic stem cell populations (HSPCs) that may manifest in hematological improvements in the clinical setting. A U.S. patent describing the synergistic activity of rigosertib in combination with azacitidine has been issued.

SymBio, Onconova's Partner in Japan and Korea, Presents Phase 1 data Demonstrating Oral Rigosertib as a Single Agent

E-Poster: A Multicenter, Open-label, Phase 1 Clinical Study; Safety, Efficacy, and Pharmacokinetics of Oral Rigosertib in Japanese Patients with Recurrent/Relapsed or Refractory MDS

A multicenter, open-label, Phase 1 clinical study of oral rigosertib (primary endpoint was dose-limiting toxicity) indicated that the recommended dose for a Phase 2 clinical study is 560 mg BID in a 2-out-of-3-week administration scheme in Japanese patients with recurrent/relapsed or refractory MDS. This regimen of oral rigosertib was well tolerated.

The primary endpoint of the study was dose-limiting toxicity. The secondary endpoints were 1) safety as assessed by adverse events and laboratory results, 2) efficacy as defined by the International Working Group 2006 Criteria, and 3) pharmacokinetics. Both hematological remission rate and hematological improvement rate were 11.1% of the nine patients with a median age of 70. In this study, the recommended dose was 560 mg BID. This study and a companion Phase 1 study with IV rigosertib were designed to obtain pharmacokinetics, safety, tolerability and efficacy data in MDS patients in Japan. Currently, SymBio is enrolling patients in a pivotal Phase 3 INSPIRE global study to assess the safety and efficacy of IV rigosertib.

Publication: Safety, Efficacy and Pharmacokinetics of Intravenous Rigosertib in Japanese Patients with Recurrent/Relapsed or Refractory MDS; A Multicenter, Open-label, Phase 1 Study

A multicenter, open-label, Phase 1 study of intravenous rigosertib was conducted to evaluate its safety, efficacy, and pharmacokinetics and to determine the recommended dose (RD) for Japanese patients.

The Phase 1 study showed that intravenous rigosertib (1,800 mg daily) for consecutive 72 hours was well-tolerated, indicating that this is the RD for Japanese patients with MDS, similar to a Phase 3 study in the U.S. Based on these clinical outcomes, Japanese patients with MDS are participating in a global randomized Phase 3 study to compare rigosertib with physicians' choice of treatment.

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 we believe 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, while causing minimal damage to normal 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 the randomized Phase 3 international INSPIRE trial for patients with higher-risk MDS, after failure of hypomethylating agent, or HMA, therapy. This formulation is intended for patients with advanced disease, provides long duration of exposure, and ensures dosing under a controlled setting.

About INSPIRE

The **IN**ternational **S**tudy of **P**hase III **I**V **R**igos**E**rtib, or INSPIRE, is based on 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. 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 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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