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Onconova Presents Phase 2 Data from Oral Rigosertib and Azacitidine Combination Trial in Higher-Risk Myelodysplastic Syndromes (HR-MDS) at 2016 ASH Annual Meeting

--35% Complete Remission (CR) Rate for Combination in 1st-line Higher-risk MDS Patients--

--Updated Median Duration of Complete Response of 8 Months in All Responding Patients--

NEWTOWN, Pa., Dec. 05, 2016 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (NASDAQ:ONTX), a clinical-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer, today announced the presentation of data from a Phase 2 clinical trial of oral rigosertib and azacitidine in higher-risk myelodysplastic syndromes (HR-MDS) at the 58th American Society of Hematology (ASH) Annual Meeting in San Diego, California.

"The complete remission rate amongst HMA-naïve HR-MDS patients is higher and responses occur more rapidly and durably with the oral rigosertib combination compared to historic single-agent azacitidine," commented Lewis R. Silverman, M.D., lead investigator in the trial and Associate Professor of Medicine, Hematology and Medical Oncology, at the Icahn School of Medicine at Mount Sinai. "Furthermore, the addition of oral rigosertib to azacitidine does not substantially change the adverse event profile of single-agent azacitidine, and thus may overcome the limitations identified in other HMA-based combinations."

The current standard of care for higher-risk MDS patients is one of two approved hypomethylating agents (azacitidine and decitabine, approved by the FDA in 2004 and 2006). Although these drugs are currently the standard of care in HR-MDS therapy, their overall response rate and duration of benefit is limited to a subset of eligible patients and all responding patients ultimately progress. Thus, there is an urgent need for improving therapeutic options for newly diagnosed HR-MDS patients. The 09-08 trial tested oral rigosertib in combination with injectable azacitidine in a dose ranging study (Phase 1), followed by an expansion cohort (Phase 2) to evaluate the efficacy and safety of the combination. Both 1st-line and 2nd-line HR-MDS patients were included in the study.

Summary of Presented Data from the 09-08 Combination Therapy Trial

Patient Demographics:

- Thirty-three of 40 MDS patients enrolled were evaluable for response at the time of this analysis.
- The median age was 66, with 73% of male patients. ECOG performance status was 0 or 1 in 95% of the patients. IPSS-R distribution was: 7.5% Low, 12.5% Intermediate, 37.5% High, 32.5% Very High and 10% unknown.

Safety/Tolerability of the Combination:

- Oral rigosertib (560 mg qAM, 280 mg qPM) was administered on Day 1-21 of a 28-day cycle. Azacitidine 75 mg/m^2/day SC or IV was administered for 7 days starting on Day 8.
- The combination of oral rigosertib and azacitidine was well tolerated.
- Adverse events of Grade ≥3 experienced across all cycles with the combination included thrombocytopenia (33%), neutropenia (30%), haematuria (13%), dysuria (8%), diarrhoea (3%) and arthralgia (3%).
- Notably, the side effects were similar to those previously reported for azacitidine administered alone.

Efficacy of the Combination:

- Thirty-three (20 HMA naïve; 13 HMA resistant) MDS patients were evaluable for efficacy analysis per IWG 2006 criteria (Cheson et al., *Blood* 2006).
- 25 of 33 (76%) patients responded per IWG — 85% of HMA naïve patients experienced a response and 62% of HMA resistant patients experienced a response.
- 7 of 20 (35%) HMA naïve and 1 of 13 (8%) HMA-resistant patients achieved a complete remission (CR). The median duration of CR was 8.0 months, which compares very favorably to the historic duration of CR and PR with single-agent azacitidine of 3.2 months[1].
- Hematologic improvement (HI) was observed in 11 of 33 patients (33%) and the median duration of response was 7.4 months for erythroid response, 8 months for platelet response, and 6.2 months for neutrophil response. Marrow CR

was observed in 16 of 33 (48%) patients and the median duration of response was 12.3 months. Marrow CR combined with HI was observed in 10 of 33 (30%) patients.

The poster entitled, "Combination of Oral Rigosertib and Injectable Azacitidine in Patients with Myelodysplastic Syndromes (MDS): Results from a Phase II Study," was presented by Dr. Shyamala Navada of Mount Sinai School of Medicine at the Myelodysplastic Syndromes Session on Sunday, December 4, 2016 at the ASH Annual Meeting in San Diego, California. A copy of the poster is available by visiting the Scientific Presentations section under the Investors & Media tab of Onconova's website.

"We are pleased by the positive efficacy signal observed over extended periods of treatment, and the acceptable tolerability of oral rigosertib and azacitidine in 1st-line HR-MDS," stated Ramesh Kumar, Ph.D., President and CEO of Onconova. "We presented Phase 2 data to the FDA as part of our End-of-Phase 2 meeting in September 2016, and based on these discussions, we are designing a randomized, placebo controlled Phase 3 clinical trial comparing the combination of oral rigosertib plus azacitidine to azacitidine plus placebo in 1st-line HR-MDS patients with the primary composite endpoint of CR and PR rate per 2006 IWG criteria. Based on our discussions with the FDA the primary efficacy endpoint of this trial will be composite response and not survival, permitting accelerated evaluation of outcomes."

Comprehensive Safety Assessment of Rigosertib in MDS Patients

In a second poster at the conference a safety review of 557 MDS/AML patients treated with rigosertib in clinical studies, including the randomized Phase 3 ONTIME trial was presented. The poster entitled, "Comprehensive Analysis of Safety: Rigosertib in 557 Patients with Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML)," can be accessed by visiting the Scientific Presentations section under the Investors & Media tab of Onconova's website.

About Onconova Therapeutics, Inc.

Onconova Therapeutics is a Phase 3 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. The Company's most advanced product candidate, rigosertib, is a small molecule inhibitor of cellular signaling and acts as a RAS mimetic. These effects of rigosertib appear to be mediated by direct binding of the compound to the RAS-binding domain (RBD) found in many RAS effector proteins, including the Raf and PI3 kinases. Rigosertib is protected by issued patents (earliest expiry in 2026) and has been awarded Orphan Designation for MDS in the United States, Europe and Japan. In addition to rigosertib, two other candidates are in the clinical stage, and several candidates are in pre-clinical stages. For more information, please visit http://www.onconova.com.

About Oral Rigosertib

The oral form of rigosertib provides a more convenient dosing for use where the duration of treatment may extend to multiple years. To date, more than 350 patients have been treated with the oral formulation of rigosertib, either as a single agent or in combination with other drugs. Phase 1 studies with 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.

About IV Rigosertib

The intravenous form of rigosertib has been employed in Phase 1, 2, and 3 clinical trial involving more than 800 patients, and is currently being evaluated in the randomized Phase 3 global INSPIRE trial as 2nd-line treatment for patients with higher-risk MDS, after failure of hypomethylating agent, or HMA, therapy. This formulation is suited for patients with advanced disease and provides long duration of exposure and ensures adequate dosing under a controlled setting.

References

[1]Fenaux et al for the international Vidaza High risk MDS survival study group, Lancet Oncology 2009, 10:223-232.

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," "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 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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