Onconova Submits Special Protocol Assessment (SPA) to FDA for Phase 3 Trial of Oral Rigosertib in Combination with Azacitidine (Vidaza®) for First-Line Myelodysplastic Syndromes (MDS)

January 2, 2019

- SPA submitted to the FDA before year-end 2018, marking achievement of a key regulatory milestone
- Advancement of this Phase 3 program, in treatment-naïve higher risk first-line MDS patients, positions rigosertib in an expanded patient population with a more convenient mode of administration
- 2019 focus remains on the completion of the pivotal INSPIRE trial studying intravenous rigosertib in second-line higher-risk MDS, while advancing business development connected to the progress of both oral and intravenous rigosertib

NEWTOWN, Pa., Jan. 02, 2019 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (NASDAQ:ONTX), a Phase 3-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer, with a primary focus on MDS, today announced that it has submitted a Special Protocol Assessment request to the U.S. Food and Drug Administration (FDA) for a Phase 3 study of oral rigosertib combination therapy with azacitidine (Vidaza®) for the treatment of adult patients with treatment-naïve higher-risk MDS. The request is part of the Company's ongoing interaction with the FDA, following an End-of-Phase 2 Meeting with FDA guidance for the proposed Phase 3 study and Scientific Advice from the European Health Authorities, consistent with the Company's strategy to study rigosertib in an earlier higher-risk MDS patient population with a more convenient mode of oral rigosertib administration. The End-of-Phase 2 Meeting also outlined that the primary endpoint of the proposed pivotal trial will be overall response rate (ORR), a composite of complete remission (CR), and partial remission (PR) based on the IWG Response Criteria.

Dr. Steve Fruchtman, President of Onconova, commented: "We remain focused in 2019 on the completion of the pivotal INSPIRE trial studying intravenous rigosertib in higher-risk MDS after patients fail to respond to or progress on hypomethylation therapy, the standard of care. The timely achievement of this regulatory milestone of this SPA submission is an important step in advancing the development of rigosertib for patients with earlier stage higher-risk MDS. We believe that the promising data in hand, including the data from the Phase 2 expansion trial of oral rigosertib and azacitidine presented at this year's 2018 ASH Annual Meeting, provides a strong scientific rationale for the proposed Phase 3 program. As the INSPIRE trial continues to mature, we look forward to a constructive engagement with the FDA on future studies. We also aim to help fund these additional studies through expanding our partnerships."

The FDA's SPA process fosters dialogue between the FDA and clinical trial sponsors before studies commence, in an attempt to reach potential agreement with the agency on the design and size of clinical trials, to determine if they adequately address the scientific and regulatory requirements for a study to ultimately support marketing approval. The Company expects its dialogue with the FDA on this SPA submission to conclude in H1 2019.

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. 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

Intravenous 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 Higher Risk-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 study 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 combination therapy modalities. To date, more than 400 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, chemotherapy or radiotherapy 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. The results of an expanded Phase 2 trial of oral rigosertib combination therapy with azacitidine were presented at the 2018 ASH Annual Meeting. This novel combination is the subject of an issued U.S. patent with earliest expiration in 2028. Additional patents covering oral and injectable rigosertib have been issued in the US, and are expected to provide coverage until at least 2037.

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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