Onconova Achieves Over 75 Percent of Planned Enrollment in Pivotal Phase 3 INSPIRE Study of Rigosertib in Myelodysplastic Syndromes

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- *Full enrollment of 360 patients anticipated in second half of 2019*
- *Pivotal global study continues enrolling worldwide*
- *Potential for first new therapy in 15 years to address unmet medical need in MDS*

NEWTOWN, Pa., March 25, 2019 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (Nasdaq: ONTX), a Phase 3 stage biopharmaceutical company focused on discovering and developing small molecule drug candidates to treat cancer today announced that it has surpassed the 75 percent enrollment milestone in its pivotal Phase 3 trial of rigosertib for the potential treatment of high-risk myelodysplastic syndromes (HR-MDS), a study known as INSPIRE.

“We are pleased to have passed the 75 percent completion of enrollment milestone and are on track with our anticipated timeline for completion of accrual to the INSPIRE study in the second half of 2019,” said Dr. Richard Woodman, Onconova’s Chief Medical Officer and Senior Vice President of Research & Development. “Rigosertib has the potential to be the first new MDS treatment in more than 15 years for a condition afflicting an estimated 59,000 patients in the United States.”

Dr. Steven M. Fruchtman, President and CEO of Onconova, stated, “Clinical execution including completing our INSPIRE study remains our top priority. In addition to near-term milestones for the INSPIRE study, we are advancing business development discussions and remain on track to reach other important clinical milestones throughout 2019 and into 2020. This includes advancing our oral rigosertib program in MDS. We are grateful to patients and to our valued partners for their participation in the important INSPIRE study, and look forward to completing patient enrollment later this year.”

The INSPIRE study is a Phase 3, open label, randomized, controlled, international study designed to determine the efficacy, safety and tolerability of single agent intravenous (IV) rigosertib to treat second-line higher-risk MDS patients. The trial includes patients under the age of 82 who have progressed on, relapsed, or failed to respond to previous treatment with hypomethylating agent (HMA) therapy within nine cycles over the course of one year after initiation of HMA therapy. Patients are randomized to receive either rigosertib with best supportive care, or the physician’s choice of therapy with best supportive care. The primary endpoint of the study is the sequential analysis of overall survival of all randomized patients in the intent-to-treat population, and the International Prognostic Scoring System - Revised (IPSS-R) Very High-Risk subgroup. Based on the promising survival signal observed by the Independent Data Monitoring Committee at interim analysis in early 2018, the Committee recommended that the trial continue with an expansion in enrollment to 360 patients based on a pre-planned sample size re-estimation.

Persons interested in participating in the INSPIRE study can obtain more information by visiting https://clinicaltrials.gov/ct2/show/NCT02562443.

About Myelodysplastic Syndromes

Myelodysplastic syndromes (MDS) are conditions that can occur when the blood-forming cells in the bone marrow become dysfunctional and thus produce an inadequate number of circulating blood cells. It is frequently associated with the presence of blasts or leukemic cells in the marrow. This leads to low numbers of one or more types of circulating blood cells, leading to the need for blood transfusions. In MDS, some of the cells in the bone marrow are abnormal (dysplastic) and may have genetic abnormalities associated with them. Different cell types can be affected, although the most common finding in MDS is a shortage of red blood cells (anemia). Patients with higher-risk MDS may progress to the development of acute leukemia.

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). 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 Rigosertib

Rigosertib, Onconova’s lead candidate, is a proprietary Phase 3 small molecule agent. A key publication demonstrated rigosertib’s ability to block cellular signaling by targeting RAS effector pathways (Divakar, S.K., et al., 2016: "A Small Molecule RAS-Mimetic Disrupts RAS Association with Effector Proteins to Block Signaling." Cell 165, 643). Onconova is currently in the clinic with oral and IV rigosertib, including single agent IV rigosertib in second-line high-risk MDS patients (pivotal Phase 3 INSPIRE trial) and oral rigosertib plus azacitidine in first-line high-risk MDS patients (Phase 2).

About IV Rigosertib

The intravenous form of rigosertib has been studied in Phase 1, 2, and 3 clinical trials involving more than 1000 patients, and is currently being evaluated in a randomized Phase 3 international INSPIRE trial for patients with high-risk MDS (HR-MDS), after failure of hypomethylating agent, or HMA, therapy.

About the INSPIRE Phase 3 Clinical Trial

The **IN**ternational **S**tudy of **P**hase 3 **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 global 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. An interim analysis in early 2018 demonstrated a promising survival signal in the intent-to-treat population as reviewed by the Independent Data Monitoring Committee. The 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, over 400 patients have been studied with the oral formulation of rigosertib. Combination therapy of oral rigosertib with azacitidine, the standard of care in HR-MDS, has also been studied. 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 efficacy and safety data was presented at The American Society of Hematology Annual Meeting in December 2018. A pivotal Phase 3 study design is under review by the FDA, and the Special Protocol Assessment is expected to conclude in the 1H of 2019. 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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