Onconova Therapeutics Announces Publication of Preclinical Data Supporting Rigosertib's Mechanism of Action as a Targeted Anticancer Therapy

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NEWTOWN, Pa., July 23, 2020 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (NASDAQ: ONTX), a Phase 3-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer, with an initial focus on myelodysplastic syndromes (MDS), today announced the publication (Molecular Cell 79, 180-190, 2020) of in vitro data further supporting rigosertib's role in modulating RAS cellular signaling.

"We believe this data sheds light on the capacity of Onconova's targeted anti-cancer agent rigosertib to modulate the RAS pathway," said Steven M. Fruchtman, M.D., President and CEO. "Mutations of the RAS pathway are the most common mutations observed in cancer. In our opinion this paper confirms the rationale to investigate rigosertib in the treatment of RAS-driven malignant diseases which continue to have a high unmet medical need. Onconova looks forward to further showcasing efforts with this novel compound, including our virtual presentation at the 2nd Annual RAS-Targeted Drug Development Summit September 14-16, 2020."

The study compared the composition and activity of non-clinical grade rigosertib with clinical grade rigosertib that is approved for investigational use in humans. The authors found that non-clinical grade rigosertib used in in vitro studies by others contained impurities and degradation products in sufficient quantities to impact cellular function. In contrast, clinical grade rigosertib, which has been used in all clinical studies to-date, is free of this impurity. Using vincristine as a control, the ability of both compounds to bind tubulin (a mechanism of action seen in less targeted chemotherapy agents) was then measured. In vitro assay results indicated that both non-clinical grade rigosertib and the vincristine control showed tubulin binding activity, while clinical-grade rigosertib did not exhibit detectable tubulin-binding activity. Furthermore, cell lines expressing mutant beta-tubulin remained sensitive to rigosertib.

"We believe that the impurities found in non-clinical grade rigosertib, but not clinical-grade rigosertib, are responsible for the cellular effects observed such as tubulin disruption. Impurities are often found in non-clinical grade products and hence the reason these materials are not permitted in clinical trials," said Richard C. Woodman, M.D., Chief Medical Officer. "The peer-reviewed data reported in *Molecular Cell* provide new detail on how these impurities can influence chemical properties, cellular functions and subsequently, potential anticancer pathways. It is our opinion that this data supports rigosertib's mechanism of action as a modulator of RAS signaling."

"Rigosertib is a RAS mimetic that binds to RAS binding domains of RAS effectors and inhibits growth of tumor cells in pre-clinical models. Our studies showed that clinical grade rigosertib does not exhibit tubulin binding activity. Clinical studies conducted by Onconova Therapeutics are expected to provide further insights into the clinical potential of this novel compound," added E. Premkumar Reddy, PhD, Professor of Pharmacological and Oncological Sciences, The Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai, who is also on Onconova's Board of Directors.

About Rigosertib

Rigosertib, Onconova's lead candidate, is a proprietary Phase 3 small molecule. A key publication in a preclinical model reported 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 clinical development stage with oral and IV rigosertib, including clinical trials studying single agent IV rigosertib in second-line higher-risk MDS patients (pivotal Phase 3 INSPIRE trial) and oral rigosertib plus azacitidine in HMA-naive and refractory higher-risk MDS patients (Phase 2). Investigator-initiated study (IIS) programs exploring oral rigosertib in a variety of cancers with mutations of RAS and its pathway are ongoing in solid tumors. Patents covering oral and injectable rigosertib have been issued in the US and are expected to provide coverage until at least 2037.

About Onconova Therapeutics, Inc.

Onconova Therapeutics, Inc. is a Phase 3-stage biopharmaceutical company focused on discovering and developing novel drugs to treat cancer, with an initial focus on myelodysplastic syndromes (MDS). Onconova has a pipeline of proprietary targeted agents designed to work against specific cellular pathways that are important in cancer cells. 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. Onconova has conducted trials with two other research compounds and has a pre-clinical program with a CDK4/6 and ARK5 inhibitor, ON 123300.

For more information, please visit https://www.onconova.com.

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, maintain its Nasdaq listing,

the need for additional financing, the success and timing of Onconova's clinical trials and regulatory approval of protocols, our collaborations including the effective termination of the HanX license and securities purchase agreements and plans for partnering certain territories, 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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