April 21, 2016

Onconova Announces Publication Describing Unique RAS-targeted Mechanism of Action for Rigosertib in the Journal Cell

-- More than 30% of all human cancers driven by RAS, a target previously considered "undruggable"--

-- Study shows rigosertib inactivates RAS signaling --

NEWTOWN, Pa., April 21, 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 that researchers from the Icahn School of Medicine at Mount Sinai, led by Professor E. Premkumar Reddy, scientific founder of Onconova, have published a study describing the novel RAS-targeted mechanism of action for rigosertib in the journal *Cell*. The paper, titled "A small molecule RAS-mimetic disrupts RAS association with effector proteins to block signaling," can be accessed in the current online edition of Cell.

RAS represents one of the most sought-after targets in cancer. Thus far the development of drugs to block RAS has been difficult, leading many to label RAS the undruggable oncogene.

"This discovery is the culmination of my laboratory's work with RAS genes over the last three decades," said Dr. E. Premkumar Reddy, lead author of the paper and Professor of Oncological Sciences at the Icahn School of Medicine at Mount Sinai. "RAS genes have been a challenging target for molecular oncologists and drug developers. However, the allosteric mechanism by which rigosertib blocks activation of signaling proteins downstream of RAS may represent a new paradigm for attacking this oncogene."

The research published in *Cell* and carried out by a multidisciplinary team from Mount Sinai, The Scripps Cancer Research Institute, Albert Einstein College of Medicine, and the New York Structural Biology Center, demonstrated that rigosertib blocks RAS signaling by directly binding to various RAS effector proteins, including RAF and PI3-kinase. These mechanistic findings support the development of rigosertib in malignancies with over-activate RAS signaling, such as higher-risk myelodysplastic syndromes (HR-MDS). Onconova is actively enrolling patients in the global INSPIRE trial, a randomized Phase 3 study to assess the efficacy and safety of single-agent intravenous rigosertib in HR-MDS.

About Rigosertib

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 kinases and PI3K. The initial therapeutic focus for rigosertib is myelodysplastic syndromes (MDS), a group of bone marrow disorders characterized by ineffective formation of blood cells that often converts into acute myeloid leukemia (AML). Clinical trials for rigosertib are being conducted at leading institutions in the United States, Europe, and the Asia-Pacific region. 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.

About RAS

Point mutations in RAS genes (HRAS, KRAS and NRAS) are frequently observed in many of the most common and lethal tumors, including cancers of the pancreas, lung, colon, skin, bladder and bone marrow. RAS genes encode important intracellular proteins that when mutated activate pathways involved in cancer cell proliferation, survival and metastasis. Although molecular oncologists have made significant headway in understanding RAS mutations and their impact on cellular signaling, less progress has been made towards developing RAS-targeted drugs. Thus, there is an urgent need for new therapeutic modalities that address this important oncogene.

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. In addition to rigosertib, the Company's most advanced product candidate, two other candidates are clinical stage, and several candidates are in pre-clinical stages. For more information, please visit http://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, 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," "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 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.

CONTACT: Onconova Therapeutics
Benjamin Hoffman, 267-759-3036
bhoffman@onconova.us