Onconova Therapeutics Announces the Peer-Reviewed Publication of Preclinical Data Demonstrating the Synergistic Anti-Cancer Activity of Rigosertib Combined with Immune Checkpoint Blockade

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Rigosertib synergistically combined with immune checkpoint blockade (ICB) to improve tumor growth inhibition and survival in a murine melanoma model that did not respond to ICB alone

Rigosertib's anti-cancer activity was due to its ability to reverse immunosuppressive tumor microenvironments

Data support the clinical evaluation of rigosertib in combination with immune checkpoint inhibitors

NEWTOWN, Pa., June 17, 2021 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (NASDAQ: ONTX) ("Onconova"), a clinical-stage biopharmaceutical company focused on discovering and developing novel products for patients with cancer, today announced the publication of a preclinical study in the journal *Molecular Cancer*. The study, entitled "Novel induction of CD40 expression by tumor cells with RAS/RAF/PI3K pathway inhibition augments response to checkpoint blockade," showed that rigosertib synergistically enhanced the efficacy of ICB in a murine melanoma model via the induction of immune-mediated cancer cell death.

"The data from this recent publication demonstrate rigosertib's potential to address a pressing unmet need, as many patients do not respond to immune checkpoint blockade due to immunosuppressive tumor microenvironments," said Ann Richmond, Ph.D., Ingram Professor of Pharmacology and Medicine at the Vanderbilt University School of Medicine and lead author of the study. "By reversing immunosuppressive tumor microenvironments, rigosertib overcame pro-tumor resistance mechanisms and synergistically enhanced the efficacy of immune checkpoint blockade in a difficult-to-treat murine melanoma model. These compelling findings provide preclinical proof-of-concept for rigosertib-immune checkpoint blockade combination therapy and strongly support its evaluation in clinical trials."

Key data and conclusions from the recent publication include:

- Rigosertib treatment enhanced the activation of anti-cancer immune cells and increased the frequency of these cells in the tumor microenvironment (TME).
- Rigosertib treatment reduced the frequency of pro-tumor CD206+ M2-like macrophages in the TME.
- Rigosertib monotherapy rapidly reduced PI3K signaling with induction of CD40 expression, leading to melanoma cell death and inhibition of tumor growth in vivo due to its ability to promote the tumor infiltration of activated anti-cancer immune cells.
- Rigosertib's ability to remodel the TME enabled it to synergistically combine with ICB and improve tumor growth inhibition and survival in a mouse model of melanoma that did not respond to ICB alone, or a clinically used combination of ICB plus BRAF and MEK inhibitors.

Steven M. Fruchtman, M.D., President and Chief Executive Officer of Onconova, added, "We are very pleased with these recently published results, which will inform the data driven approach guiding our clinical rigosertib investigator-initiated study program. They provide strong mechanistic support for both the ongoing KRAS mutated non-small cell lung cancer trial of rigosertib in combination with a check point inhibitor and a potential trial in patients with advanced melanoma evaluating a rigosertib-checkpoint inhibitor combination that is under active consideration. Looking ahead, we plan to continue leveraging our collaborations with leading institutions such as Vanderbilt University as we pursue opportunities for rigosertib while maintaining our primary focus and resources on our lead ON 123300 multi-kinase inhibitor program."

About Onconova Therapeutics, Inc.

Onconova Therapeutics is a clinical-stage biopharmaceutical company focused on discovering and developing novel products for patients with cancer. The Company has proprietary targeted anti-cancer agents designed to disrupt specific cellular pathways that are important for cancer cell proliferation.

Onconova's novel, proprietary multi-kinase inhibitor ON 123300 is being evaluated in two separate and complementary Phase 1 dose-escalation and expansion studies. These trials are currently underway in the United States and China.

Onconova's product candidate rigosertib is being studied in an investigator-initiated study program, including in a dose-escalation and expansion Phase 1 investigator-initiated study targeting patients with KRAS+ non-small cell lung cancer with oral rigosertib in combination with nivolumab. In addition, Onconova continues to conduct preclinical work investigating rigosertib in COVID-19.

For more information, please visit 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's expectations regarding the timing of Onconova's and investigator-initiated clinical development plans, and the mechanisms and indications for Onconova's product candidates. 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 the success and timing of Onconova's clinical trials and regulatory agency and institutional review board approvals of protocols, the timing of the Company's annual stockholder meeting, market conditions 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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