Onconova Therapeutics Announces Dosing of First Participant in Investigator-Sponsored Phase 2 Trial of Rigosertib Plus Pembrolizumab in Metastatic Melanoma Patients Refractory to Immune Checkpoint Blockade

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NEWTOWN, Pa., May 25, 2023 (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 that the first participant has been dosed in an investigator-sponsored Phase 2 trial of oral rigosertib plus the PD-1 inhibitor pembrolizumab in patients with metastatic melanoma who have progressed on prior PD-1/L1 inhibitor therapy.

"There is an urgent need for new treatment approaches in metastatic melanoma, as 40 to 60% of these patients currently see little to no clinical benefit from PD-1 inhibitors," said Ann Richmond, Ph.D., Ingram Professor of Pharmacology and Medicine at the Vanderbilt University School of Medicine and Senior Research Career Scientist at TVHS, Department of Veterans Affairs (Nashville). "The limited efficacy of these agents is often due to 'cold' tumor microenvironments (TME) that prevent the infiltration of immune effector cells. Peer-reviewed preclinical studies[1] suggest rigosertib can enhance the efficacy of immune checkpoint blockade in metastatic melanoma by reversing cold TMEs, providing a strong scientific rationale for this clinical trial."

Douglas B. Johnson, M.D., M.S.C.I., Associate Professor of Medicine of Hematology/Oncology at Vanderbilt University Medical Center and Principal Investigator of the trial commented, "Rigosertib combined with anti-PD-1 therapy has shown clinical activity in checkpoint inhibitor refractory lung cancer patients, and we believe this promising finding may translate to melanoma. The newly initiated Phase 2 study has been thoughtfully designed to begin exploring this hypothesis and will afford participants the opportunity to receive a novel therapeutic combination that may lead to improved clinical outcomes. I look forward to conducting the study and to the important scientific insights I expect it will provide."

The investigator-sponsored Phase 2 trial is an open-label, two-stage, single arm study. Stage 1 of the trial is expected to include ten patients. If a pre-specified response criteria is met, the study will then proceed to Stage 2, during which an additional 19 patients are expected to be enrolled. Patients in the study will receive 560 mg of oral rigosertib twice daily on days 1-21 of 28-day treatment cycles, plus 400 mg of pembrolizumab administered via intravenous infusion every six weeks. The primary endpoint of the trial is overall response rate, while key secondary endpoints include assessments of safety, tolerability, progression-free survival, and overall survival. Correlative biomarker assessments will also be conducted.

Steven M. Fruchtman, M.D., President and Chief Executive Officer of Onconova, commented, "Rigosertib's investigator-sponsored trials are an important component of our corporate strategy that allows us to diversify the indications studied with our pipeline while remaining internally focused on our lead narazaciclib program. We are thrilled to be collaborating with Vanderbilt's world-class physician-scientists on this latest trial and look forward to its advancement."

For additional information on the Phase 2 trial, see Clincialtrials.gov identifier NCT05764395.

References:

1. Yan, C., Saleh, N., Yang, J. et al. Novel induction of CD40 expression by tumor cells with RAS/RAF/PI3K pathway inhibition augments response to checkpoint blockade. *Mol Cancer* **20**, 85 (2021). https://doi.org/10.1186/s12943-021-01366-y.

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 narazaciclib (formerly ON 123300) is being evaluated in a combination trial with estrogen blockade in advanced endometrial cancer. Based on preclinical and clinical studies of CDK 4/6 inhibitors, Onconova is also evaluating opportunities for combination studies with narazaciclib in additional indications.

Onconova's product candidate rigosertib is being studied in multiple investigator-sponsored studies. These studies include a dose-escalation and expansion Phase 1/2a study of oral rigosertib in combination with nivolumab in patients with KRAS+ non-small cell lung cancer, a Phase 2 program evaluating rigosertib monotherapy in advanced squamous cell carcinoma complicating recessive dystrophic epidermolysis bullosa (RDEB-associated SCC), and a Phase 2 trial evaluating rigosertib in combination with pembrolizumab in patients with metastatic melanoma.

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 its clinical development and trials, its product candidates, its business

and financial position. Onconova has attempted to identify forward-looking statements by terminology including "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," “preliminary,” “encouraging,” "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, investigator-initiated trials and regulatory agency and institutional review board approvals of protocols, Onconova’s collaborations, 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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