Onconova Therapeutics Provides an Update on the Phase 1/2a Trial of Rigosertib-Nivolumab Combination in KRAS+ Non-Small Cell Lung Cancer

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Expansion of trial underway at highest dose in the current protocol, and continued dose escalation under consideration

Preliminary data support the preclinical observation of rigosertib augmenting the response to immune checkpoint inhibition

NEWTOWN, Pa., June 28, 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 an update on the investigator-initiated Phase 1/2a trial of oral rigosertib plus nivolumab in advanced metastatic KRAS mutated (KRAS+) non-small cell lung cancer (NSCLC). The clinical data to date provide preliminary evidence of potential anti-cancer activity of rigosertib-nivolumab combination therapy in advanced metastatic KRAS+ non-small cell lung cancer and show that the maximum tolerated dose of rigosertib in combination with nivolumab was not reached in the three cohorts of the trial's dose-escalation phase. Patients enrolled in this trial have failed multiple lines of prior therapy and all have failed immune checkpoint inhibitors in various combinations.

The trial continues to recruit patients as part of the expansion phase at the highest dose of oral rigosertib defined in the current protocol. Based on the positive preliminary findings from the trial, a protocol amendment is being prepared that would allow for the evaluation of increased rigosertib doses in combination with the full dose of intravenous nivolumab, as recommended per its product label.

"The preliminary results from this Phase 1/2a trial are very encouraging and demonstrate the potential of rigosertib to address a critical unmet medical need by overcoming checkpoint inhibitor resistance in KRAS mutated lung adenocarcinoma," said Mark S. Gelder, M.D., Chief Medical Officer of Onconova. "The observation of preliminary evidence of efficacy in combination with acceptable safety of the doublet in this extremely challenging patient population provides a promising signal. This phase 1 study supports the preclinical observation in melanoma of the up regulation of crucial cell surface molecules by rigosertib which may synergize with immune checkpoint blockade, as recently published in *Molecular Cancer*, and strongly supports the continued clinical development of rigosertib-checkpoint inhibitor combination therapy. We look forward to the presentation of preliminary data at the upcoming 3rd Annual RAS Targeted Drug Development Summit taking place September 21-23, 2021, and at a future major medical meeting as the data mature."

Steven M. Fruchtman, M.D., President and Chief Executive Officer of Onconova, commented, "This Phase 1/2a trial is an important part of our investigator-initiated study program, which enables us to pursue opportunities to develop rigosertib in high-need KRAS mutated indications while maintaining our primary focus on our lead ON 123300 program. We are very pleased both with the safety and preliminary efficacy signal we have seen from the KRAS mutated NSCLC trial to date, considering the multiple lines of therapy many of these patients have previously failed, including checkpoint inhibitors in various combinations. We are supportive of the plan to expand dose-escalation of rigosertib to determine the optimal recommended Phase 2 dose of the combination; and are eagerly anticipating results of important correlative science that is part of the trial. We look forward to the trial's continued progress and would like to thank the investigator and his team for conducting the trial, as well as the patients who are participating."

About the Investigator-initiated Phase 1/2a Trial
This Phase 1/2a trial is designed to evaluate the combination of rigosertib and nivolumab in advanced KRAS+ metastatic lung adenocarcinoma patients who have progressed on standard of care with anti-PD-1 monotherapy or anti-PD-1 in combination with chemotherapy. It includes a dose-escalating Phase 1 portion followed by a Phase 2a dose-expansion portion. Patients in the trial receive oral rigosertib twice daily on days 1-21, and intravenous nivolumab on days 1 and 15 of 28-day cycles. The primary endpoints of the trial are safety assessments and overall response rate. Secondary endpoints include progression free survival and overall survival. For more information on the trial, see ClinicalTrials.gov Identifier: NCT04263090.

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 1/2a 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

and data presentation 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, investigator-initiated trials and regulatory agency and institutional review board approvals of protocols, Onconova's collaborations, 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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