Onconova Therapeutics Announces Updated Data from Investigator-sponsored Phase 1/2a Trial Evaluating Rigosertib in Combination with Nivolumab in Advanced KRAS-mutated Non-Small Cell Lung Cancer at the ESMO Congress 2022

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- *Data show an early signal of efficacy in an extensively pre-treated population with 1 complete response and 2 partial responses achieved in 14 evaluable patients*
- *Responses achieved in patients with 3 distinct and different KRAS mutations, confirming the MOA of rigosertib being KRAS+ agnostic*
- *4 of 14 (29%) evaluable patients demonstrated disease control*
- *The combination of rigosertib and nivolumab has been well tolerated with no synergistic toxicities observed to-date*

NEWTOWN, Pa., Sept. 12, 2022 (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 updated data from an investigator-sponsored Phase 1/2a trial of oral rigosertib plus the anti-PD-1 immune checkpoint inhibitor (ICI) nivolumab in advanced KRAS-mutated (KRAS+) non-small cell lung cancer (NSCLC). The data, which are featured in a poster at the European Society for Medical Oncology (ESMO) Congress 2022, show an early and encouraging signal of efficacy in the trial's extensively pre-treated population. The studied doublet has been well tolerated to-date.

"The emerging data being presented at ESMO are encouraging, as treatment with rigosertib plus nivolumab led to both complete and partial responses in patients with KRAS-mutated lung cancers who failed prior ICI therapy," said Dr Rajwanth Veluswamy, the principal investigator of the study. "Objective responses showcased rigosertib's KRAS mutation-agnostic mechanism of action, as each responding patient had a tumor with a different underlying variant. This differentiates rigosertib from agents targeting a single KRAS mutation variant, and positions it to potentially address the unmet needs of a much broader patient population. In addition, the ESMO data demonstrated activity in multiple patients with both low PD-L1 expression at diagnosis and STK11/LKB1 co-mutations, both poor predictive features for current lung cancer treatments."

Key data from the presentation include:

Demographics:

- All enrolled patients failed at least one line of prior therapy with a PD-1 checkpoint inhibitor (includes evaluable and non-evaluable patients)
- 80% of enrolled patients failed at least two lines of prior therapy

Response results (as of August 15th, 2022-data cutoff date):

- 3 of 14 evaluable patients achieved an objective response
  - 1 patient achieved a complete response (CR) as per RECIST Criteria, with complete resolution of the primary lung tumor as well as sites of metastatic disease.
  - 2 patients achieved a partial response (PR)
  - Responses were achieved in patients with 3 distinct KRAS mutations (CR: KRAS G12V; PRs: KRAS G12C/STK11 and Q61H/STK11)
- The mean duration of response is 6.75 months
- 4 of 14 evaluable patients achieved disease control (CR, PR, or stable disease)

Safety results:

- The studied doublet has been generally well tolerated. Treatment-related adverse events (TRAE) have been mostly mild and manageable.

- One dose limiting toxicity of grade 3 hyponatremia has been observed (previously documented with rigosertib)
- Urinary toxicities well documented with rigosertib are the most common TRAE
- No unexpected safety events or synergistic toxicities have been observed

Steven M. Fruchtman, M.D., President and Chief Executive Officer of Onconova, commented, “The evidence of efficacy observed in the trial’s highly challenging population suggests rigosertib may synergize with ICI and potentially provide clinical benefit to patients with limited therapeutic options. This hypothesis is supported both by these latest clinical data and the results of preclinical studies in multiple indications. Looking forward, we expect the maturation of the trial’s current results, as well as the new data we expect to collect by enrolling additional patients, to provide key insights that will inform the next steps for rigosertib’s current investigator-sponsored study program.”

The ESMO poster (#1018P) is titled “Phase 1/2 Trial of Rigosertib and Nivolumab for KRAS Mutated Non-Small Cell Lung Cancer (NSCLC) Patients.” It is currently available for viewing on the congress’s virtual platform and is being presented by the trial’s principal investigator, Rajwanth Veluswamy, M.D., Assistant Professor, Medicine, Hematology and Medical Oncology, Icahn School of Medicine at Mount Sinai, today during Poster Session 14. The poster is available on the “Scientific Presentations” section of the Onconova website.

About the Investigator-sponsored Phase 1/2a Trial

This Phase 1/2a trial is designed to evaluate the combination of rigosertib and nivolumab in advanced KRAS+ metastatic NSCLC 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 to determine maximum tolerated dose, 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 narazaciclib (formerly 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-sponsored study program, including in a dose-escalation and expansion Phase 1/2a investigator-sponsored study with oral rigosertib in combination with nivolumab for patients with KRAS+ non-small cell lung cancer.

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 trial data, and the mechanisms, therapeutic effects, 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," “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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