



**ONCONOVA**  
THERAPEUTICS

## **Onconova Therapeutics Presents Preclinical Data Characterizing Rigosertib's Mechanisms of Action at the AACR Targeting RAS Conference**

March 7, 2023

*Data suggest rigosertib stimulates an anti-cancer immune response via NLRP3 activation, providing mechanistic support for clinical trials of rigosertib-checkpoint inhibitor combinations*

*Data reveal potential targets engaged by rigosertib to inhibit the RAS-MAPK pathway, the overactivation of which is implicated in a range of cancers*

NEWTOWN, Pa., March 07, 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, announced new preclinical data characterizing rigosertib's mechanisms of action in a poster at the American Association for Cancer Research Special Conference on Targeting RAS (AACR Targeting RAS Conference).

"The preclinical results presented at the Targeting RAS Conference increase our understanding of rigosertib's anti-cancer effects and thereby represent a valuable tool to inform its continued clinical development," said Mark Gelder, M.D., Chief Medical Officer of Onconova. "I am particularly encouraged by data showing rigosertib-induced activation of the NLRP3 inflammasome. These data provide additional support for [previously reported clinical results](#) in KRAS-mutated non-small cell lung cancer that suggest rigosertib can synergize with checkpoint inhibition to drive clinical response in patients with various KRAS mutations that failed prior checkpoint inhibitor therapy. Data identifying potential targets through which rigosertib inhibits RAS-MAPK signaling are also compelling, as this pathway plays a key role in the formation and growth of a variety of cancers. Collectively, these data provide a mechanistic rationale for the differentiated potential of rigosertib when compared to the FDA approved agents that target only the KRAS G12C mutation."

Preclinical studies featured in the poster evaluated mechanisms by which rigosertib may activate an anti-cancer immune response and inhibit the RAS-MAPK pathway. Results indicate that rigosertib stimulates an immune response via activation of the NLRP3 inflammasome, which leads to the secretion of the pro-inflammatory cytokines IL-1 $\beta$  and IL-18. Additional data identified the proteins NQO2, ERO1A, and NEK7 as potential novel targets that may be modulated by rigosertib. Activation of NQO2 and/or ERO1A leads to reactive oxygen species (ROS)-induced activation of JNK signaling, which in-turn leads to RAS-MAPK pathway inhibition. Rigosertib interaction with NEK7 could possibly cause the destabilization of microtubules and cell cycle arrest in mitosis, which are critical for cell division.

A copy of the poster, titled "CETSA Profiling Unveils Novel Targets Engaged by Anti-tumor Drug Rigosertib to Inhibit RAS-MAPK Signaling and Trigger NLRP3 Inflammasome Activation," is available on the "[Scientific Presentations](#)" section of the Onconova website.

### **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. Based on preclinical and clinical studies of CDK 4/6 inhibitors, Onconova is also planning a combination trial of narazaciclib with estrogen blockade in advanced endometrial cancer, as well as its clinical study in additional indications.

Onconova's product candidate rigosertib is being studied in multiple investigator-sponsored studies, including 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, and a Phase 2 program evaluating rigosertib monotherapy in advanced squamous cell carcinoma complicating recessive dystrophic epidermolysis bullosa.

For more information, please visit [www.onconova.com](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, 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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