Onconova Therapeutics Announces the Presentation of New Preclinical Data on Narazaciclib at the AACR Annual Meeting

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Data further characterize narazaciclib's mechanism of action and show its anti-cancer activity comparing favorably to that of FDA-approved CDK 4/6 inhibitors

NEWTOWN, Pa., April 19, 2023 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (NASDAQ: ONTX), ("Onconova" or "the Company"), a clinical-stage biopharmaceutical company focused on discovering and developing novel products for patients with cancer, today announced new preclinical data on narazaciclib in two poster presentations at the American Association for Cancer Research (AACR) Annual Meeting.

"Data being presented at AACR further highlight how narazaciclib's differentiated inhibitory profile may allow it to overcome the shortcomings of FDA-approved CDK 4/6 inhibitors," said Steven M. Fruchtman, M.D., President and Chief Executive Officer of Onconova. "Kinases recently identified as targets of narazaciclib, but not of the most widely prescribed CDK 4/6 inhibitor include BUB1, the overexpression of which was shown to be associated with poor survival in subtypes of endometrial and breast cancer. In addition, data featured in the AACR posters provide additional evidence of narazaciclib's potential to combine synergistically with therapeutic agents in a variety of drug classes. Looking forward, the learnings from these studies will be a valuable asset as we advance narazaciclib's Phase 1/2a trial in endometrial cancer and evaluate potential opportunities for its clinical study in additional indications and with combination approaches to promote efficacy in resistant tumors."

Poster 5987: Differential targets engaged by narazaciclib in comparison to the approved CDK 4/6 inhibitors contribute to enhanced inhibition of tumor cell growth.

Featured in this poster are data characterizing narazaciclib's mechanism of action and activity in preclinical cancer models. Results showed that, in addition to inhibiting kinases such as CDK 4/6, narazaciclib treatment led to the degradation of other kinases not targeted by the FDA-approved CDK 4/6 inhibitor palbociclib. These kinases included BUB1, the overexpression of which was shown to be associated with poor prognosis in breast cancer and uterine corpus endometrial carcinomas. Data from PYMT murine breast cancer cells showed a stronger induction in apoptosis (programmed cell death) with narazaciclib compared to palbociclib and another FDA-approved CDK 4/6 inhibitor, abemaciclib. In addition, data from multiple cell lines suggest that inhibiting autophagy may sensitize breast cancer cells to narazaciclib treatment.

Poster 5974: Synergistic activity of the CDK 4/6 antagonist narazaciclib (ON123300) with irreversible BTK inhibition in ibrutinib-resistant mantle cell lymphoma.

Data featured in this poster demonstrate narazaciclib's potent antitumor activity against mantle cell lymphoma (MCL) cell lines, independent of their sensitivity to the FDA-approved Bruton's tyrosine kinase inhibitor ibrutinib. Narazaciclib's activity against MCL cell lines was shown to be superior to that of the FDA-approved CDK 4/6 inhibitors palbociclib and ribociclib, and similar to that of the FDA-approved CDK 4/6 inhibitor abemaciclib. Combining narazaciclib with ibrutinib led to synergistic increases in antitumor activity against both ibrutinib-sensitive and ibrutinib-resistant MCL cell lines. In addition, narazaciclib exhibited significant antitumor activity without detectable toxicity when combined with ibrutinib in an *in vivo* model of MCL (embryo chorioallantoic membrane xenograft model).

Copies of the AACR posters will be available on the on the "Scientific Presentations" section of the Onconova website following the conclusion of the conference.

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 (RDEB-associated SCC).

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.

Company Contact:
Mark Guerin
Onconova Therapeutics, Inc.
267-759-3680
ir@onconova.us
https://www.onconova.com/contact/

Investor Contact:
Bruce Mackle
LifeSci Advisors, LLC
646-889-1200
bmackle@lifesciadvisors.com