Onconova Therapeutics Announces Abstract at the ASCO Annual Meeting Highlighting Narazaciclib's Differentiated Inhibitory and Improved Safety Profile in Preclinical Models

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In vitro and cell-based assays suggest narazaciclib's inhibitory profile may provide safety and efficacy advantages over currently approved CDK4/6 inhibitors

NEWTOWN, Pa., May 26, 2022 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (NASDAQ: ONTX), a clinical-stage biopharmaceutical company focused on discovering and developing novel products for patients with cancer, today announced the publication of an abstract at the American Society of Clinical Oncology (ASCO) Annual Meeting. Featured in the abstract are preclinical data from *in vitro* and cell-based assays that demonstrate how narazaciclib's inhibitory profile differentiates it from the FDA-approved CDK4/6 inhibitors palbociclib, ribociclib, and abemaciclib.

Key data and conclusions from the abstract include:

- Narazaciclib, abemaciclib, palbociclib, and ribociclib each have strong affinity for CDK4/cyclin D1, with K_d values of 0.18 nM, 0.08 nM, 0.75 nM, and 1.3 nM, respectively.
- Narazaciclib and abemaciclib have similar affinities against CDK family members, including nM activity against CDK2/cyclin A, which may play a role in resistance to palbociclib and ribociclib.
- Narazaciclib's inhibitory activity against GSK3β, a kinase whose inhibition putatively causes tolerability issues related to diarrhea, is ~29 times less than that of abemaciclib.
- Cellular kinase assays showed narazaciclib's highest inhibitory activity to be against CDK4/6, CSF1R, (supports pro-tumor immune suppression), and NUAK1/ARK 5 (associated with poor prognosis in multiple cancers and implicated in cancer cell migration, invasion, and metastasis).
- Cellular Thermal Shift Assay (CETSA) and integrative Inferred Kinase Activity (INKA) analysis showed that narazaciclib is associated with and modulated unique signaling pathways resulting in specific deregulated phosphorylation patterns when compared to palbociclib treated cells.

Steven M. Fruchtman, M.D., President and Chief Executive Officer of Onconova and co-author of the abstract, commented, "Though revolutionary and commercially successful, currently available CDK4/6 inhibitors are limited by tolerability and safety issues as well as the unfortunate reality of primary and acquired drug resistance. This creates a pressing unmet need for novel agents that may overcome these shortcomings and provide patients with durable clinical benefit. Narazaciclib's decreased affinity for targets associated with poor tolerability, together with its increased inhibitory activity against kinases implicated in metastasis, cancer cell survival, immune suppression, and drug resistance, suggests it may address this need. We continue to explore this hypothesis in narazaciclib's clinical program and remain on track to establish a recommended Phase 2 dose by the end of the year."

A copy of the abstract, titled, "Narazaciclib's kinase inhibitory activity is differentiated from approved CDK4/6 inhibitors in preclinical models," is available on the ASCO Annual Meeting website.

About Onconova Therapeutics

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 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," "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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