Onconova Therapeutics Files Investigational New Drug Application for Multi-kinase CDK4/6 Inhibitor ON 123300

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- U.S. Phase 1 trial patient enrollment to begin in the first half of 2021
- China Phase 1 trial enrollment ongoing
- Key regulatory milestone achieved to enable further study of product candidate for patients with HR+ HER 2- metastatic breast cancer and other tumors

NEWTOWN, Pa., Nov. 23, 2020 (GLOBE NEWSWIRE) -- **Onconova Therapeutics, Inc. (NASDAQ: ONTX)**, a biopharmaceutical company focused on discovering and developing novel products to treat cancer, today announced the filing of an Investigational New Drug application (IND) with the U.S. Food and Drug Administration (FDA) for ON 123300, the Company's proprietary, differentiated, first-in-class multi-kinase inhibitor. The IND seeks permission to begin a Phase 1 trial with ON 123300 in relapsed/refractory advanced cancer including patients with HR+ HER 2- metastatic breast cancer with resistance to approved second-generation CDK4/6 inhibitors.

"We believe that ON 123300, based on its novel mechanism of action, presents an innovative approach to study advanced cancers including in HR+ HER 2- metastatic breast cancer that is or has become resistant to commercial CDK4/6 inhibitors. We are delighted to have filed our IND on schedule, and look forward to enrolling patients in the U.S. to complement the ongoing Phase 1 dose-escalation study underway in China by our partner HanX Biopharmaceuticals," said Steven M. Fruchtman, M.D., President and Chief Executive Officer of Onconova. "The HanX Phase 1 ON 123300 study, which began in September 2020, has enrolled three patients to date and is expected to continue to enroll patients with advanced relapsed/refractory cancer at two sites until the recommended Phase 2 dose is identified. We believe that data from these two studies will generate important information to inform anticipated later-stage studies."

As currently envisioned, the Phase 1 trial in the U.S. will assess the safety, tolerability, and pharmacokinetics of ON 123300 administered orally as monotherapy at increasing doses starting at 40 mg daily or higher for consecutive 28-day cycles. The Phase 1 trial is planned for patients with relapsed/refractory advanced cancer, including but not limited to patients with HR+ HER 2- metastatic breast cancer with clinical resistance to the approved second-generation CDK4/6 inhibitors. Once the recommended Phase 2 dose is established, the Company's plan is to enroll additional HR+ HER 2- postmenopausal metastatic breast cancer patients refractory to approved second-generation CDK4/6 inhibitors, as well as patients diagnosed with advanced non-Hodgkin's lymphoma with a special interest in mantle cell lymphoma.

This trial design in the U.S. differs from the study in China because HanX is dosing patients daily for 21 days. Notably, of the three currently approved CDK4/6 inhibitors, two are approved for dosing in 21-day cycles and one is approved for dosing in a 28-day cycle. All three are blockbuster drugs marketed by well-known pharmaceutical companies, and all of these approved therapies require concomitant treatment with an aromatase inhibitor.

"Beyond metastatic breast cancer, we believe that ON 123300 may present an innovative approach to treating other cancers including mantle cell lymphoma, multiple myeloma, advanced colorectal cancer, advanced hepatocellular carcinoma, and inoperable glioblastoma based on preclinical studies suggesting ON 123300 crosses the blood-brain barrier," added Richard Woodman, M.D, Chief Medical Officer.

Commenting on the expected timetable and next steps with this program, Dr. Fruchtman added: "Once the FDA approves our IND, we will seek Institutional Review Board approval at the site where this Phase 1 trial will be conducted. We anticipate the first patient to be enrolled during the first half of 2021. With the ON 123300 program advancing, investigator-sponsored trials underway with our pipeline product rigosertib, and an active business development campaign to evaluate additional compounds, we look forward to an expanding portfolio of novel therapeutics for large, underserved oncology indications."

About ON 123300

Onconova's lead pipeline product is the novel small molecule ON 123300, a proprietary, first-in-class multi-kinase inhibitor targeting tumor-driving kinases including CDK4/6 and ARK5. ON 123300 is reported to simultaneously inhibit both cell cycle and cellular energy metabolism through CDK4/6 and ARK5, respectively, and *in vitro* has been shown to be cytotoxic to cancer cells (killing the cancer cells) rather than just cytostatic (inhibiting the growth of cancer cells), which is how the currently commercial CDK inhibitors are reported to work. With its differentiated mechanism of action, ON 123300 may present an innovative approach for treating solid tumors and hematologic malignancies that are refractory to or have become resistant to other CDK4/6 inhibitors.

Based on experiments in preclinical models, ON 123300 exhibits single-agent cytotoxicity, may have utility for certain types of cancers including breast cancer and non-Hodgkin's lymphoma, and may also have utility for mantle cell lymphoma, multiple myeloma, advanced colorectal cancer, advanced hepatocellular carcinoma, and inoperable glioblastoma.

About Onconova Therapeutics, Inc.

Onconova Therapeutics is a biopharmaceutical company focused on discovering and developing novel products to treat 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 currently in a dose-escalation and expansion Phase 1 trial in China, and an IND has been filed in the U.S. Onconova's product candidate oral rigosertib is currently in a dose-escalation and expansion Phase 1 investigator-initiated study targeting patients with KRAS+ lung adenocarcinoma in combination with nivolumab. Preclinical work with rigosertib in COVID-19 is ongoing as well. Although some preclinical experiments with rigosertib in cellular models demonstrated marked inhibition of SARS-CoV-2 replication, we do not anticipate conducting clinical trials with rigosertib in COVID-19 without securing additional funding. 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 patents and clinical development plans including patient enrollment timelines and indications for its 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 and regulatory agency and institutional review board approvals of protocols, Onconova's ability to continue as a going concern, the need for additional financing, Onconova's collaborations, 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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