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Onconova Highlights Data on Novel Mechanism and Pharmacokinetics of Lead Compound ON 01910.Na at AACR

APRIL 16, 2010 – NEWTOWN, PA AND PRINCETON, NJ -- Onconova Therapeutics, Inc. today announced four scientific presentations regarding ON 01910.Na at the Annual Meeting of the American Association for Cancer Research (AACR), being held April 17-21 in Washington, D.C. The data will be presented on Monday and Tuesday during the meeting.

Two presentations provide additional insight into the novel mechanism of action of ON 01910.Na, a unique anti-cancer molecule currently in Phase I and II clinical trials at several major centers in the USA and abroad for solid tumors and hematological cancers. A pivotal approval-track trial for ON 01910.Na in myelodysplastic syndromes (MDS) is planned to start this summer.

These studies highlight on the novel mode of action of ON 01910.Na and provide information of pharmacokinetic and *in vivo* disposition parameters. ON 01910.Na has been administered to more than 250 cancer patients in clinical trials. These trials have been carried out with ON 01910.Na as a single agent or in combination with Eloxatin® (oxaliplatin) or Gemzar® (gemcitabine). Additional information on these trials is available at www.clintrials.gov.

AACR Presentations Concerning ON 01910.Na:

Monday, April 19, 2:00 – 5:00 PM

Abstract #2500

“ON 01910.Na, a clinical stage anticancer mitotic inhibitor, produces prolonged hyperphosphorylation of RanGAP1•SUMO1 as a potential mechanism of G2/M arrest and apoptosis.”

Oussenko I, Holland JF, Reddy EP & Ohnuma T.

Session Title: Anticancer Drugs Targeting Cell Cycle and Proliferation

Location: Exhibit Hall A-C, Poster Section 21

Session Category: Experimental and Molecular Therapeutics 16

Irina Oussenko, Ph.D., and colleagues at Mt. Sinai School of Medicine provide a potential molecular explanation of the mitotic arrest caused by ON 01910.Na. These researchers assessed

DNA damage checkpoints throughout the cell cycle in several tumor cell lines. ON 01910.Na did not activate DNA damage-responsive molecules Chk1, Chk2, or ATM. Instead, hyperphosphorylation of RanGAP1•SUMO1 was observed. These findings show that ON 01910.Na is neither a direct DNA damage response inducer nor a tubulin toxin, and suggest that ON 01910.Na inhibits RanGAP1•SUMO1 phosphatase, leading to prolonged hyperphosphorylation of RanGAP1•SUMO1, causing G2/M arrest and apoptosis.

Abstract #2766

“Multicenter Pharmacokinetic Evaluation of ON 01910.Na, a novel broad-spectrum anticancer agent, in Phase I Single Agent Clinical Trials in Patients with Solid Tumors.”

Maniar M, Mani S, Ghalib M, Chaudhary I, Roboz J, Ohnuma T, Advani S, Rao R, Doval D, Acharya M, O'Rourke E, Wilhelm F, Holland JF & Taft DR.

Session Title: Pharmacokinetic, Pharmacogenomic, and Clinical Results of Early-Phase Trials

Location: Exhibit Hall A-C, Poster Section 33

Session Category: Clinical Research 11

Manoj Maniar, Ph.D., of Onconova, describes detailed analysis of pharmacokinetics of ON 01910.Na in 81 advanced cancer patients from six centers receiving ON 01910.Na at various infusion rates, durations, and doses. ON 01910.Na showed biphasic elimination from the plasma, regardless of dose and administration schedule. ON 01910.Na clearance was lower at higher drug dosing rates and the functional half-life, estimated from initial decline of plasma levels following infusion termination, was less than 2 hours. These data suggest that continuous intravenous infusion could be employed to provide prolonged, well-tolerated exposure to ON 01910.Na.

Tuesday, April 20, 9:00 AM -12:00 PM

Abstract #3493

“ON 01910.Na, a clinical trial stage multi-kinase inhibitor, induces apoptosis in chronic lymphocytic leukemia (CLL) cells through inhibition of PI3K/AKT and activation of the JNK pathway resulting in NOXA and BIM upregulation.”

Perez-Galan P, Chapman C, Sun X, Gibellini F, Liu P, Raghavachari N & Wiestner A.

Session Title: Combinatorial Approaches to Therapy

Location: Exhibit Hall A-C, Poster Section 21

Session Category: Experimental and Molecular Therapeutics 22

Patricia Perez-Galan, Ph.D., and colleagues at the National Heart, Lung and Blood Institute, NIH, studied selective apoptosis induced by ON 01910.Na in chronic lymphocytic leukemia (CLL) samples *in vitro*. ON 01910.Na-treated CLL cells exhibited activated pro-apoptotic Bax and Bak proteins, leading to mitochondrial depolarization and cell death. Gene expression profiling revealed a dual mechanism of action: inhibition of the PI3K/AKT survival pathway and

induction of oxidative stress, which resulted in upregulation of Noxa, a protein promoting cell death. These data, and the relative safety of ON 01910.Na against normal T and B lymphocytes, have supported a clinical trial at the NHLBI, which is now enrolling patients.

Abstract #3534

“Proposed Pathway of Disposition of ON 01910.Na, a Novel Clinical Trial Stage Anti-Cancer Agent: Implication of Mrp2 in Biliary Excretion in the Isolated Perfused Rat Liver System.”

Taft DR, Chun AW, Ren C & Maniar M.

Session Title: Mechanisms of Resistance 4: Drug Transporters and Chemotherapeutics

Location: Exhibit Hall A-C, Poster Section 23

Session Category: Experimental and Molecular Therapeutics 24

David Taft, Ph.D, of Long Island University, presents studies on the disposition of ON 01910.Na in an isolated perfused rat liver (IPRL) model. Extensive biliary excretion in the IPRL system was noted, and biliary transport appeared to be mediated in part by Mrp2 protein. IPRL findings correlated well with *in vivo* studies in rats, demonstrating the utility of the IPRL model in drug development.

About Onconova’s Product Pipeline

Onconova is developing therapeutic candidates directed at critical targets involved in signal transduction, cell-cycle, and DNA repair. These candidates are derived from the Company’s proprietary library of new chemical entities and non-ATP competitive chemotypes. In addition to ON 01910.Na, Onconova is also developing Ex-RAD™, an injectable and oral radioprotectant, and inhibitors of Cyclin D, JAK, and Bcr-abl pathways.

About Onconova Therapeutics, Inc.

Onconova, based in Newtown, PA and Princeton, NJ, discovers and develops novel small molecule therapeutic agents for cancer, radiation protection, and hematological disorders. Currently, the Company is conducting clinical trials at major centers in the USA and abroad for three product candidates. The novel chemical library platform is permitting identification of kinase inhibitors directed at validated and novel targets, and exploring a new immunoconjugate technology (comprising potent active compounds and proprietary linkers) for arming monoclonal antibodies for cancer therapy. All of the Company’s products and technologies are being developed internally.

For more information on Onconova Therapeutics, Inc., please visit www.onconova.com.

Ex-RAD™ trademark is registered to Onconova Therapeutics, Inc.