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Onconova Therapeutics Announces Positive Preclinical Data for Third-Generation Oral CDK4/6 + ARK5 Inhibitor and dual FLT3 and Src inhibitor at 2017 American Association for Cancer Research (AACR) Annual Meeting

- Comparative biological studies with Palbociclib
- Single-agent activity of ON 123300 in various models including multiple myeloma and lymphoma

NEWTOWN, Pa., April 04, 2017 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (Nasdaq: ONTX), a Phase 3 stage biopharmaceutical company focused on discovering and developing small molecule drug candidates to treat cancer, with a primary focus on Myelodysplastic Syndromes, announced promising pre-clinical data for first-in-class dual inhibitor of CDK4/6 + ARK5, as well as a Type 1 novel inhibitor of FLT3 and Src pathways as a novel strategy for Acute Myeloid Leukemia (AML) therapy at the 2017 AACR Annual Meeting. The Company presented its findings in two poster presentations on April 3, 2017.

ON 123300, an orally administered novel CDK4/6 + ARK5 inhibitor, exhibits potent antitumor activity in vivo: comparative studies with Palbociclib

ON 123300, a third-generation potent CDK4/6 inhibitor that also inhibits ARK5 with low nanomolar potency, was found to be as effective as Palbociclib (Pfizer's Ibrance®) in an Rb + ve xenograft model. Moreover, the molecule may have the potential advantage of reduced neutropenia when compared to Palbociclib. Both compounds decreased RBC and platelet counts, however in this model system, Palbociclib had a more prominent and statistically significant ($P \leq 0.05$) inhibitory effect on neutrophil counts when compared to ON 123300 (30.70 ± 3.55 vs. 45.10 ± 2.04).

"There is a need for next-generation CDK4/6 inhibitors such as ON 123300, given the limitations of second-generation compounds that depend on a second molecule for therapeutic use. We are particularly excited about ON 123300 because of its potential to act as a single agent, as a dual inhibitor of CDK 4/6 + ARK 5 and which could be suitable for indications that may not be amenable to Palbociclib-like compounds," said Dr. Ramesh Kumar, CEO of Onconova.

A full copy of the above AACR poster can be accessed by visiting "Scientific Presentations" in the Investors and Media section of Onconova's website.

Dual inhibition of FLT3 and Src pathways by ON 150030, a type 1 inhibitor, as a novel strategy for relapsed and refractory AML

Biological studies at the Icahn School of Mount Sinai reveal that ON 150030 specifically inhibits the growth of MV4-11 cells harboring the FLT3-ITD mutation (GI50: 10nM). Western blot analysis demonstrates that MAPK and PI3K/AKT pathways in these cells are inhibited with increasing dose of ON 150030. The JAK independent phosphorylation of STAT5 seen in the context of FLT3-ITD is also reduced in response to ON 150030. The poor survival rate among FLT3-ITD positive AML patients and the resistance associated with current treatment regimens highlight a need for a novel FLT3 inhibitor that will be effective in cells resistant to Quizartinib.

"We are excited by the positive data on these two preclinical compounds, which address dual targeting strategy to address difficult to treat diseases. These promising results underscore the depth of our clinical pipeline, which is led by rigosertib, an advanced Phase 3 stage innovation for the treatment of patients with myelodysplastic syndromes. Following the advancement of our late stage trials in 2016, rigosertib is positioned for multiple key milestones in 2017," concluded Dr. Kumar.

About Onconova Therapeutics, Inc.

Onconova Therapeutics, Inc. is a Phase 3 stage biopharmaceutical company focused on discovering and developing novel small molecule drug candidates to treat cancer, with a primary focus on Myelodysplastic Syndromes (MDS). Rigosertib, Onconova's lead candidate, is a proprietary Phase 3 small molecule agent, which blocks cellular signaling by targeting RAS effector pathways. Using a proprietary chemistry platform, Onconova has created a pipeline of targeted agents designed to work against specific cellular pathways that are important in cancer cells, while causing minimal damage to normal cells.

Onconova has three product candidates in the clinical stage and several pre-clinical programs. Advanced clinical trials with our lead compound, rigosertib, are aimed at what we believe are unmet medical needs of patients with MDS. For more information, please visit http://www.onconova.com.

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