

## **Studies on Curaxin CBL0137 in preclinical models of pancreatic cancer**

November 14 2014

Cleveland BioLabs, Inc. and Roswell Park Cancer Institute (RPCI) today announced the publication of studies in Oncotarget describing the preclinical efficacy of Curaxin CBL0137 as a single agent and in combination with the current standard-of-care therapy, gemcitabine, against different models of pancreatic ductal adenocarcinoma (PDA), including models of gemcitabine-resistant tumors. The reported studies were conducted by scientists at Roswell Park, SUNY Downstate Medical Center and Buffalo Biolabs, LLC.

Pancreatic cancer is the fourth leading cause of cancer-related death in the United States and is one of the few cancers for which survival has not improved substantially over nearly 40 years. Pancreatic cancer has the highest mortality rate of all major cancers; 94% of pancreatic cancer patients will die within five years of diagnosis (American Cancer Society: Cancer Facts & Figures 2014).

CBL0137 is a small molecule that modulates several important signaling pathways involved in the pathogenesis of PDA through inhibition of chromatin remodeling complex, also known as FACT. FACT has recently been shown to be a novel target in cancer due to its frequent overexpression in multiple tumor types Tumor cells, but not normal cells, are dependent on FACT function for survival FACT-positive tumors are associated with an aggressive malignant phenotype (highgrade, metastatic disease, worse overall survival) Research has shown that FACT is expressed in the majority of cases of PDA One of the most significant factors predisposing patients to PDA is chronic pancreatic



inflammation accompanied by constitutive activity of NF-kappaB In addition, the heat shock response stress pathway, which is mediated by HSF1, is also frequently overactive in PDA cells Inhibition of FACT inhibits cellular stress pathways mediated by NF-kappaB and HSF-1,3,4 FACT inhibition also activates the pro-apoptotic factor p53.

In the published studies, the effect of CBL0137 monotherapy or in combination with gemcitabine was evaluated using patient-derived PDA xenografts and PANC-1 orthotopic tumors. In addition, potential mechanisms for the combined efficacy observed between CBL0137 and gemcitabine were investigated. CBL0137 was efficacious against mouse models of PDA and enhanced the effect of gemcitabine by causing a significant delay in tumor relapse following the completion of treatment. The data presented in the publication suggest that these combined effects may be a result of CBL0137 targeting of PDA cancer stem cells, as well as its modulation of the expression of genes that affect gemcitabine sensitivity in PDA cells. CBL0137 also demonstrated anti-tumor effects in models of gemcitabine-resistant tumors.

A Phase 1 trial assessing the intravenous administration of Curaxin CBL0137 in patients with metastatic or unresectable advanced solid cancers and lymphomas is underway in multiple centers in the United States, including RPCI. A Phase 1 study assessing the oral administration of Curaxin CBL0137 in patients with advanced solid tumors that are resistant or refractory to current standard treatment is being conducted in several centers in the Russian Federation.

Wen Wee Ma, MBBS, Associate Professor of Oncology in the Department of Medicine at RPCI and Principal Investigator for the intravenous trial of CBL0137, stated, "Pancreatic cancer is a very challenging disease that is highly resistant to conventional chemotherapy. CBL0137 has been shown to be effective in preclinical pancreatic cancer models, including gemcitabine-resistant tumors. The agent seems to



target pancreatic cancer stem cells and survival pathways, thus rendering this a very promising treatment for this disease."

Andrei Gudkov, PhD, DSci, Senior Vice President of Basic Science at Roswell Park Cancer Institute and Chief Scientific Officer of Cleveland BioLabs, commented, "These data reinforce our growing base of evidence regarding the potentially broad efficacy of Curaxin CBL0137's mechanism of action. The data shared in this publication and the known role of FACT in the pathogenesis of PDA and viability of cancer stem cells support our consideration of <u>pancreatic cancer</u> as a potential indication for Phase 2 development of CBL0137."

**More information:** The Oncotarget publication may be found online at: <u>impactjournals.com/oncotarget/ ... &op=view&path[]=2701</u>

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