Novel therapeutic candidate targets key driver of HCC in genomically defined subset of patients

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Findings were presented today at The International Liver Congress 2015 on a novel therapeutic candidate for a genomically defined subset of hepatocellular carcinoma (HCC) patients with an aberrant fibroblast growth factor receptor 4 (FGFR4) pathway. BLU-554, a small molecule inhibitor of FGFR4, has been identified as a potential treatment option for up to 30% of HCC patients. In preclinical studies, the investigational drug was shown to be potent and 'exquisitely selective' for FGFR4 compared to other kinases targeting the FGFR family.

Overexpression of fibroblast growth factor 19 (FGF19), the ligand for FGFR4, can promote liver tumour formation (as observed in genetically-engineered mice), a process that can be blocked by knocking out the FGFR4 gene. This suggests that FGFR4 inhibition might be an effective treatment strategy in HCC patients whose tumours have an active FGF19/FGFR4 signalling axis.

The study authors found that BLU-554 had significant anti-tumour activity in liver cancer models that are dependent on FGFR4 signalling pathway and was well tolerated at the highest dose level.

Klaus Hoeflich, PhD, Director of Biology at Blueprint Medicines, explains: "HCC is a disease with a high unmet need and no approved genomically targeted therapies. These findings support the investigation of BLU-554 in clinical studies of patients with hepatocellular carcinoma

driven by aberrant FGFR4 signalling. By identifying patients most likely to respond to therapy based on the molecular profile of their cancer, we hope to make a meaningful difference for HCC patients."

With limited treatment options available to patients with HCC, these findings provide a new avenue of hope; Phase I clinical trials with BLU-554 are planned to start in mid-2015.

"Most people are diagnosed with hepatocellular carcinoma once the cancer is at an advanced stage and the outlook is poor. Median survival from time of diagnosis is about six months. Finding new disease drivers and treatment options for patients with hepatocellular carcinoma is critical to make strides against this devastating disease" said Dr Laurent Castera, Vice-Secretary, European Association for the Study of the Liver.

More information: FIRST SELECTIVE SMALL MOLECULE INHIBITOR OF FGFR4 FOR THE TREATMENT OF HEPATOCELLULAR CARCINOMAS WITH AN ACTIVATED FGFR4 SIGNALING PATHWAY, The International Liver Congress 2015.

Provided by European Association for the Study of the Liver