Blueprint Medicines Publishes Preclinical Proof-of-Concept Data on Promising New Therapy for Patients with Genomically Defined Hepatocellular Carcinoma

- *On track to file IND for BLU-554 and initiate clinical studies by mid-2015* -

CAMBRIDGE, Mass., March 16, 2015 - Blueprint Medicines today announced publication of the discovery and preclinical characterization of BLU9931, a selective, covalent inhibitor of fibroblast growth factor receptor 4 (FGFR4). The publication highlights the significant anti-tumor activity of BLU9931 in several *in vivo* models of hepatocellular carcinoma (HCC) with aberrantly active signaling of FGFR4. FGFR4, together with its ligand FGF19, are validated genomic drivers in up to one third of liver cancer patients. The discovery of BLU9931 led to the identification of a lead drug BLU-554 with improved pharmaceutical properties which Blueprint Medicines intends to advance into clinical trials in mid-2015. Data were published electronically in the most recent edition of *Cancer Discovery*, a journal of the American Association of Cancer Research (Hagel M. et al., "First selective small molecule inhibitor of FGFR4 for the treatment of hepatocellular carcinomas with an activated FGFR4 signaling pathway").

"The profound anti-tumor activity of these exquisitely selective kinase drugs demonstrates promising preclinical proof-of-concept in a disease with high unmet need and no approved genomically targeted therapies," said Andy Boral, M.D., Ph.D., Senior Vice President, Clinical Development at Blueprint Medicines. "These data, combined with the encouraging results of the 28-day GLP-compliant toxicology studies and our novel genomics approach to identifying patients most likely to respond to our therapy, warrant exploring clinical proof-of-concept trials with our lead drug BLU-554 in HCC patients."

The *Cancer Discovery* publication outlines the unique discovery process led by Blueprint Medicines' scientists to craft selective, covalent drugs to FGFR4, which historically had been a challenging kinase for drug discovery due to the sequence similarities with the other FGFR paralogs. In the publication, BLU9931 demonstrates:

- Greater than fifty-fold selectivity for FGFR4 relative to other FGFR family members and little to no inhibition of all other kinases;
- Dose-dependent tumor growth inhibition in a HCC cell-line xenograft model harboring genomic amplification of FGFR4 pathway components. Tumor-bearing mice experienced a complete remission for 30-days after cessation of 21-day treatment; and
- Dose-dependent tumor growth inhibition in a patient-derived HCC xenograft model, which is believed to be predictive of clinical response. BLU-554 demonstrated superior efficacy compared to sorafenib, the only systemic treatment currently approved for HCC patients.

The publication also features the genomics analysis conducted by Blueprint Medicines to investigate the molecular mechanisms underlying aberrant activation of FGFR4 signaling and confirmed the prevalence in up to one third of HCC patients.

Blueprint Medicines expects to initiate Phase I clinical trials with BLU-554 in mid-2015 and is currently preparing an Investigational New Drug (IND) application for the U.S. Food and Drug Administration.

About Blueprint Medicines

Blueprint Medicines makes kinase drugs to treat patients with genomically defined diseases. Led by a team of industry innovators, Blueprint Medicines integrates a novel target discovery engine and a proprietary compound library to understand the blueprint of cancer and craft highly selective therapies. This empowers the Blueprint Medicines team to develop patient-defined medicines aimed at eradicating cancer. Blueprint Medicines is privately held and raised $115 million in financing since its 2011 inception.

About Hepatocellular Carcinoma

Liver cancer is the second leading cause of cancer-related deaths worldwide, with hepatocellular carcinoma (HCC) accounting for most liver cancers. The highest incidence of HCC occurs in regions with endemic hepatitis B virus, including Southeast Asia and sub-Saharan Africa. In the United States, HCC is the fastest rising cause of cancer-related death; over the past two decades, the incidence of HCC has tripled while the five-year survival rate has remained below 12%. Treatment options for advanced HCC are limited and there are currently no treatments that target genomically defined patient populations.

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