Blueprint Medicines Presents New Preclinical Data Demonstrating Its Drug Candidate BLU-554 Induces Significant Tumor Regression in Models of Hepatocellular Carcinoma

– Company on track to file IND and initiate Phase 1 clinical trial in mid-2015 –

CAMBRIDGE, Mass., April 24, 2015 – Blueprint Medicines today announced new preclinical data demonstrating that BLU-554, a selective and potent inhibitor of fibroblast growth factor receptor 4 (FGFR4), has significant anti-tumor activity in models of hepatocellular carcinoma (HCC) that are dependent on FGFR4 signaling. A highly targeted therapeutic candidate, BLU-554 induced complete tumor regression in a subset of mice harboring genomic amplification of an FGFR4-activating ligand at the highest dose levels. These data will be presented today at the 50th International Liver Congress™ (ILC) 2015 in Vienna, Austria, and have been chosen by the European Association of the Study of the Liver (EASL) to be highlighted in an ILC press conference.

"Patients with advanced HCC face a grim prognosis, and there is a desperate need for effective new treatments," said Josep M. Llovet, MD, Director of the Mount Sinai Liver Cancer Program and Professor of Medicine at Mount Sinai School of Medicine at New York University and Professor of Research-ICREA in the BCLC Group, Liver Unit, IDIBAPS-Hospital Clínic of Barcelona. "The genomic profiling of liver cancer has lagged behind that of other tumor types, but we are now gaining new insights that are paving the way for highly targeted therapies like BLU-554 for defined subsets of patients based on the molecular blueprint of their cancers."

BLU-554 showed significant anti-tumor efficacy and was well-tolerated in two *in vivo* models of HCC driven by aberrant FGFR4 signaling, one with genomic amplification of FGFR4-activating ligand FGF19 and another with FGF19 overexpression in the absence of amplification. In the preclinical data being presented at ILC, BLU-554 demonstrated:

- Complete tumor regression in 100 percent of mice with genomic amplification of FGF19 treated for 21 days at the 100 mg/kg twice daily and 200 mg/kg once daily doses.
- Dose-dependent tumor growth inhibition in mice with overexpression of FGF19 in the absence of amplification.
- Potent inhibition of FGFR4 and greater than 100-fold more selectivity for FGFR4 than FGFR1-3 in *in vitro* studies. In contrast, pan-FGFR inhibitors fail to exhibit selective inhibition of FGFR4 compared with the other family members.
- Little to no inhibition of all other kinases.

Abnormal activation of FGFR4 signaling is a key driver in up to 30 percent of HCC patients. The overexpression of the FGF19 ligand triggers aberrant FGFR4 signaling, leading to cell proliferation and tumor growth. FGF19 overexpression can be caused by

genomic amplification of the FGF19 gene but also occurs in the absence of genomic amplification via other molecular mechanisms.

"By precisely and potently inhibiting a key driver of disease, BLU-554 has the potential to change the treatment paradigm for a significant portion of HCC patients," said Anthony Boral, MD, PhD, Senior Vice President of Clinical Development, Blueprint Medicines. "We are very encouraged by these data and are committed to developing this highly targeted therapy as rapidly as possible by selecting patients whose disease is driven by abnormal FGFR4 signaling and are most likely to respond to BLU-554. The selectivity of BLU-554 may also allow for combination therapy strategies to effectively treat even broader populations of HCC patients."

Blueprint Medicines has previously disclosed data on BLU9931, a selective, covalent inhibitor of FGFR4. BLU9931 led to the identification of the Company's lead drug BLU-554 with improved pharmaceutical properties. The Company is on track to file an Investigational New Drug (IND) Application and begin a Phase 1 clinical trial of BLU-554 in mid-2015 in HCC patients.

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.

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