Blueprint Medicines Presents New Preclinical Data Demonstrating Significant Anti-Tumor Activity of BLU-285 in Treatment-Resistant GIST and on Novel Cancer Drug Targets

– On track to file INDs for BLU-285 and initiate clinical studies in mid-2015 –

– Presentations at AACR Showcase Company's Ability to Identify New Drivers of Cancer and Craft Highly Selective Kinase Inhibitors for Genomically Defined Diseases –

CAMBRIDGE, Mass., April 19, 2015 – Blueprint Medicines today announced new preclinical data demonstrating that its drug candidate BLU-285 has significant anti-tumor activity in treatment-resistant models of gastrointestinal stromal tumors (GIST) and achieved and maintained complete tumor regression in all mice treated at the highest dose level. These data were presented at the American Association for Cancer Research (AACR) Annual Meeting 2015.

"Despite advances in treating GIST, there are still subsets of patients who do not respond to currently available treatments or relapse and become resistant to treatment," said Suzanne George, MD, Clinical Director, Center for Sarcoma and Bone Oncology and Senior Physician at the Dana Farber Cancer Institute and Assistant Professor of Medicine at Harvard Medical School. "By inhibiting PDGFRα D842V and KIT Exon 17 mutants, which are key drivers of treatment-resistant GIST, BLU-285 could offer a highly targeted therapy for patients who have no effective treatment options. In addition, the selectivity of BLU-285 for these mutants may allow for less off-target toxicity than currently available agents, opening the door to future combination therapy strategies."

Blueprint Medicines also presented data identifying new cancer drug targets during a minisymposium at AACR on cancer genomics. Using proprietary computational tools to identify kinase fusions involved in cancer, the Company uncovered 16 known fusions in new cancer types and identified 21 novel fusions across six genes that likely play a key role in cancer. In addition to paving the way for the discovery and development of novel therapies, these findings could have immediate implications for the diagnosis and treatment of cancer patients.

"These presentations demonstrate the power of Blueprint Medicines' discovery engine to identify promising new drug targets and craft highly selective kinase inhibitors against previously unaddressed genomic drivers of cancer," said Blueprint Medicines Chief Scientific Officer Christoph Lengauer, PhD, MBA. "Kinases play a key role in virtually every aspect of cancer, and there is tremendous untapped potential to deliver much-needed new therapies for patients with genomically defined diseases based on a deep understanding of cancer's blueprint."

BLU-285 in GIST
BLU-285 is a highly targeted drug that potently and selectively inhibits PDGFRα D842V and KIT Exon 17 mutants, which are receptor tyrosine kinase mutants known to be key drivers in treatment-resistant and metastatic GIST. Because BLU-285 binds to regions of the PDGFRα and KIT kinases that are structurally similar, it is able to simultaneously inhibit PDGFRα D842V and KIT Exon 17 mutants with minimal inhibition of other kinases, potentially limiting the off-target side effects associated with many cancer treatments.

The new preclinical data presented at AACR show that BLU-285 induces significant tumor regression in a patient-derived *in vivo* model of GIST that is refractory to treatment with imatinib, an approved first-line treatment for GIST. Key findings include:

- BLU-285 achieved and maintained complete tumor remission in 100 percent of mice treated with an oral, once daily dose of 30 mg/kg or 100 mg/kg for 28 days
- Complete tumor regression was maintained during a 28-day observation period following treatment at the 100 mg/kg dose

Blueprint Medicines is on track to file an Investigational New Drug (IND) Application and begin a Phase 1 clinical trial of BLU-285 in mid-2015 that will include GIST patients whose cancer is driven by PDGFRα D842V and KIT Exon 17 mutants. The Company also plans to file an IND and begin a Phase 1 clinical trial in mid-2015 for BLU-285 in patients with systemic mastocytosis, another disease with significant unmet need in which a KIT Exon 17 mutant plays a key role.

New Cancer Drug Targets
As part of the minisymposium, chaired by Dr. Lengauer, Blueprint Medicines presented its research findings and computational approach providing a strong genetic rationale that the newly discovered kinase fusions, as well as the known fusions in new cancer types, are genomic drivers of cancer. Fusion genes are known cancer drivers, and kinase fusions are proven cancer drug targets. A fusion gene is formed when a portion of one gene is joined to part of another gene.

Based on these findings, Blueprint Medicines is advancing one disclosed drug discovery program targeting RET, a receptor tyrosine kinase that can be abnormally activated by fusions, and predicted RET resistance mutants. The Company's scientists identified RET fusions in four of 20 cancer types analyzed, including thyroid, lung, breast and colon cancers. Although RET fusions were known to play a role in thyroid and lung cancers, the discovery that they were also drivers of colon and breast cancers was new.

The identification of novel fusions that activate known cancer-causing genes, as well as known fusions in new cancer types also has immediate implications for patients, potentially pointing to approved or exploratory therapies that would not otherwise have been considered.

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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