Blueprint Medicines Presents Preclinical Data Highlighting Broad Precision Therapy Research Pipeline at AACR Annual Meeting 2021

-- Preclinical data presented at AACR highlight four precision therapies with first- or best-in-class potential --

-- IND application cleared by FDA for BLU-945, a triple-mutant EGFR inhibitor for EGFR-driven lung cancer --

-- Nominated BLU-222, a selective and potent CDK2 inhibitor development candidate, for cyclin E-aberrant cancers --

-- Blueprint Medicines to host investor conference call and webcast on Monday, April 12 at 8:00 a.m. ET --

CAMBRIDGE, Mass., April 10, 2021 – Blueprint Medicines Corporation (NASDAQ: BPMC) today announced data from multiple poster presentations highlighting the breadth of the company's precision therapy pipeline at the virtual American Association for Cancer Research (AACR) Annual Meeting 2021. Collectively, the presentations, including foundational preclinical data for multiple programs, demonstrate the productivity of the company's scientific platform. Additional presentations of clinical data for AYVAKIT™ (avapritinib) and BLU-263 will be reported on Sunday, April 11, 2021.

"Our data presentations at the AACR annual meeting showcase Blueprint Medicines' next wave of precision therapies, which have the potential to impact large global patient populations," said Fouad Namouni, M.D., President, Research & Development at Blueprint Medicines. "Building on the foundation of our approved medicines AYVAKIT and GAVRETO®, these presentations highlight our efforts to address significant patient needs in areas such as EGFR-driven lung cancer, cyclin E-aberrant cancers and cancer immunotherapy. As we celebrate our 10th anniversary as a company, and our rapidly expanding pipeline now includes our ninth development candidate, we look forward to continuing to leverage our productive research platform to advance potent and selective inhibitors that have the potential to enable transformative benefit for patients."

BLU-701 and BLU-945: Double- and triple-mutant inhibitors in EGFR-driven NSCLC

Lung cancer is the leading cause of cancer death globally, and approximately 17 percent of patients with lung adenocarcinoma, the most common form of non-small cell lung cancer (NSCLC), have EGFR-driven disease. While first- and third-generation EGFR inhibitors have improved treatment outcomes for patients with EGFR-driven NSCLC, resistance inevitably emerges, with the T790M and C797S mutations being the most common on-target resistance mechanisms. Together, BLU-701 and BLU-945 are designed to provide comprehensive coverage of the most common activating and on-target resistance mutations, spare wild-type EGFR to limit toxicities driven by wild-type EGFR inhibition and treat or prevent central nervous system (CNS) metastases. Ultimately, with these characteristics, BLU-701 and BLU-945 have the potential to be used either as monotherapy or in combination, together or with other agents, to potentially overcome or prevent on-target resistance across multiple lines of treatment.

BLU-701 is a potential best-in-class, selective, potent, fourth-generation double-mutant EGFR inhibitor with activity against EGFR activating mutations and the C797S osimertinib-resistant mutation. Preclinical data presented at the conference showed strong and durable inhibition of tumor growth at doses that are EGFR wild-type sparing. BLU-701 also indicated significant CNS penetration in preclinical models, with comparable exposure in the plasma and brain, which illustrates its potential to treat or prevent CNS metastases in patients with EGFR-driven tumors. With activity also shown against the activating EGFR mutants, BLU-701 has potential to be used in both first- and second-line settings.

BLU-945 is a potential first- and best-in-class, selective, potent, fourth-generation triple-mutant EGFR inhibitor with activity against the T790M and C797S resistance mutations. BLU-945 is highly selective over wild-type EGFR and off-target kinases, highlighting its potential to enable tolerable combinations with BLU-701 or other therapies. Data presented at the conference demonstrated potent anti-tumor activity in triple-mutant osimertinib-resistant tumor models, as well as activity in a triple-mutant intracranial patient-derived xenograft model. In addition, the combination of BLU-945 with either gefitinib or osimertinib showed enhanced anti-tumor activity when compared with either gefitinib or osimertinib alone.

The preclinical data presented for BLU-701 and BLU-945 support the continued development of both candidates in patients with EGFR-driven NSCLC. An investigational new drug (IND) application for BLU-945 has been cleared by the U.S. Food and Drug Administration (FDA) and an international Phase 1 dose escalation trial is expected to begin this quarter. Future clinical development of BLU-945 in combination with other agents across multiple treatment settings is planned. BLU-701 is expected to enter clinical development later this year.

BLU-222: CDK2 inhibitor in cyclin E-aberrant cancers

Cyclin dependent kinases (CDKs) and their cyclin partners regulate the cell cycle. In subsets of patients across multiple cancer types, aberrant cyclin E (CCNE) hyperactivates CDK2, resulting in cell cycle dysregulation and tumor proliferation. Aberrant CCNE has been observed as a primary driver of disease as well as a mechanism of resistance to CDK4/6 inhibitors and other therapies. In addition, data have shown that ovarian and hormone-receptor-positive breast cancer patients with aberrant CCNE have poor outcomes. Prior drug discovery efforts targeting CDK2 have been hindered by challenges in achieving selectivity over other CDK family members associated with toxicity.

At AACR, preclinical data highlighted a set of potent and selective CDK2 inhibitors designed by Blueprint Medicines. The data showed that selective CDK2 inhibition arrested the cell cycle and blocked tumor proliferation in CCNE-amplified cell lines and demonstrated robust and sustained anti-tumor activity in vivo in models of CCNE-amplified ovarian, breast and gastric cancer. A selective CDK2 inhibitor also showed improved tolerability compared to a pan-CDK inhibitor and chemotherapy, as measured by animal body weight.

Based on this work and further optimization, Blueprint Medicines today announced the nomination of a potentially best-in-class selective and potent CDK2 inhibitor development candidate, BLU-222, which is expected to enter clinical development in the first half of 2022.

BLU-852: MAP4K1 inhibitor

MAP4K1 is a well-characterized immunokinase target involved in the regulation of immune cells; however, prior drug discovery efforts have been hindered by challenges in achieving selectivity over other MAP4K family members associated with toxicity. In January 2021, Blueprint Medicines announced the nomination of a highly selective and potent MAP4K1 inhibitor development candidate, BLU-852, with best-in-class potential.

Data presented at AACR highlighted a set of potent and highly selective MAP4K1 inhibitors designed by Blueprint Medicines, including BLU-852. The inhibitors were shown to enhance intratumoral immune cell activation, overcome T cell suppression, and reduce tumor burden both as a monotherapy and in combination with checkpoint inhibition. The data

support the continued development of BLU-852 under the company's cancer immunotherapy collaboration with Roche, with Phase 1 trial initiation anticipated in 2022.

Copies of Blueprint Medicines data presentations from the AACR annual meeting are available in the "Science—Publications and Presentations" section of the company's website at www.BlueprintMedicines.com.

Conference Call Information

Blueprint Medicines will host a live webcast on Monday, April 12, 2021 beginning at 8:00 a.m. ET to review data for multiple research- and clinical-stage programs presented at the AACR annual meeting. To access the live call, please dial (855) 728-4793 (domestic) or (503) 343-6666 (international) and refer to conference ID 5548976. A webcast of the conference call will be available under "Events and Presentations" in the Investors & Media section of Blueprint Medicines' website at http://ir.blueprintmedicines.com. The archived webcast will be available on Blueprint Medicines' website approximately two hours after the conference call and will be available for 30 days following the call.

About Blueprint Medicines

Blueprint Medicines is a global precision therapy company that invents life-changing medicines for people with cancer and hematologic disorders. Applying an approach that is both precise and agile, we create therapies that selectively target genetic drivers, with the goal of staying one step ahead across stages of disease. Since 2011, we have leveraged our research platform, including expertise in molecular targeting and world-class drug design capabilities, to rapidly and reproducibly translate science into a broad pipeline of precision therapies. Today, we are delivering our approved medicines to patients in the United States and Europe, and we are globally advancing multiple programs for genomically defined cancers, systemic mastocytosis, and cancer immunotherapy. For more information, visit www.BlueprintMedicines.com and follow us on Twitter (@BlueprintMeds) and LinkedIn.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding the plans, timing, designs, implementation, enrollment and announcement of results regarding Blueprint Medicines' ongoing and planned clinical trials for its drug candidates; the potential benefits of Blueprint Medicines' current and future drug candidates in treating patients; and Blueprint Medicines' strategy, goals and anticipated milestones, business plans and focus. The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks and uncertainties related to the impact of the COVID-19 pandemic to Blueprint Medicines' business, operations, strategy, goals and anticipated milestones, including Blueprint Medicines' ongoing and planned research and discovery activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved products, and launching, marketing and selling current or future approved products; Blueprint Medicines' ability and plans in establishing a commercial infrastructure, and successfully launching, marketing and selling current or future approved products,

including AYVAKIT™/AYVAKYT® (avapritinib) and GAVRETO® (pralsetinib); Blueprint Medicines' ability to successfully expand the approved indications for AYVAKIT/AYVAKYT and GAVRETO or obtain marketing approval for AYVAKIT/AYVAKYT and GAVRETO in additional geographies in the future; the delay of any current or planned clinical trials or the development of Blueprint Medicines' current or future drug candidates; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' ability to successfully demonstrate the safety and efficacy of its drug candidates and gain approval of its drug candidates on a timely basis, if at all; the preclinical and clinical results for Blueprint Medicines' drug candidates, which may not support further development of such drug candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; Blueprint Medicines' ability to develop and commercialize companion diagnostic tests for its current and future drug candidates; and the success of Blueprint Medicines' current and future collaborations, partnerships or licensing arrangements. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Blueprint Medicines' filings with the Securities and Exchange Commission (SEC), including Blueprint Medicines' most recent Annual Report on Form 10-K, as supplemented by its most recent Quarterly Report on Form 10-Q and any other filings that Blueprint Medicines has made or may make with the SEC in the future. Any forward-looking statements contained in this press release represent Blueprint Medicines' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Blueprint Medicines explicitly disclaims any obligation to update any forward-looking statements.

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