Blueprint Medicines' Continued Leadership in Redefining the Standard of Care in Systemic Mastocytosis Highlighted at 2024 ASH Annual Meeting

-- ASH data reinforce survival benefits of front-line AYVAKIT® (avapritinib) use in patients with advanced SM --

-- Bone density analyses reported in patients with advanced SM underscore disease-modifying effects of AYVAKIT --

CAMBRIDGE, Mass., December 7, 2024 – Blueprint Medicines Corporation (Nasdaq: BPMC) today announced data presentations that continue to demonstrate the long-term clinical benefits of AYVAKIT® (avapritinib) in advanced systemic mastocytosis (advanced SM), and reflect the company's ongoing partnership with the SM community to redefine the future of patient care – from improving diagnostic rates to raising the bar on treatment outcomes. The datasets, which include one oral presentation and three poster presentations, will be reported at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition, taking place December 7-10 in San Diego.

"Systemic mastocytosis is associated with mast cell infiltration across multiple organ systems, chronic inflammation caused by immune dysregulation, unpredictable symptoms that may worsen over time, and serious comorbidities such as osteoporosis, highlighting the urgency to treat patients early in the course of their disease," said Becker Hewes, M.D., Chief Medical Officer at Blueprint Medicines. "AYVAKIT has fundamentally changed the treatment paradigm by targeting the disease at its source, showing prolonged survival outcomes for patients with advanced SM, as well as durable symptom control and quality-of-life improvements for patients with ISM. Based on the substantial datasets we have amassed over more than a decade, and our continued collaboration with the SM community, we have designed the HARBOR trial of elenestinib – a next-generation KIT D816V inhibitor – to rigorously assess a broad range of endpoints reflecting disease-modifying impact."

Data reported at ASH highlight the survival benefits of front-line AYVAKIT use in patients with advanced SM, and support Blueprint Medicines' plans to evaluate novel clinical measures indicative of disease modification – such as bone density and biomarkers of chronic inflammation – in the registrational HARBOR trial. Key results include:

- In pooled analyses from the PATHFINDER and EXPLORER trials, treatment-naïve patients with advanced SM showed significant survival benefits with AYVAKIT, when indirectly compared to real-world outcomes for midostaurin.
- In the PATHFINDER trial, AYVAKIT led to sustained improvements in bone density for advanced SM patients who had low bone mass at baseline.
- In the PIONEER trial, patients with indolent SM (ISM) had significant baseline levels of immune dysregulation relative to healthy donors, reflecting the chronic inflammatory burden of the disease.

Non-Invasive, Blood-Based Assay Identified KIT Mutations Not Previously Detectable by Existing Tests

ASH data show that ultra-sensitive KIT testing in the peripheral blood – a novel tool in clinical development that is more sensitive than current commercially available methods – identified previously undetected KIT mutations in a number of PIONEER trial patients. Emerging clinical research with ultra-sensitive KIT assays suggest SM may be more prevalent than previously thought.

An additional data presentation highlights the application of machine learning techniques to analyze baseline, blood-based parameters of Blueprint Medicines' clinical trial participants. Following these analyses, a predictive model was developed to distinguish between advanced SM and ISM, and its accuracy was validated by an independent dataset from Dana-Farber Cancer Institute.

Collectively, these data build on Blueprint Medicines' collaborative efforts with clinical experts to improve and accelerate how SM is diagnosed and treated.

Data presentations will be made available in the "Science—Publications and Presentations" section of Blueprint Medicines' website.

- Oral Presentation: Analysis of Avapritinib Clinical Trial Data Generates a Highly Accurate Predictive Model for Advanced Systemic Mastocytosis Versus Indolent Systemic Mastocytosis Based on Peripheral Blood Testing *(Abstract 107 – Saturday, December 7)*
- Poster Presentation: Overall Survival and Duration of Treatment in Patients with Advanced Systemic Mastocytosis Receiving Avapritinib Versus Midostaurin or Best Available Therapy in a Real-World Setting *(Abstract 1801 – Saturday, December 7)*
- Poster Presentation: Ultra-Sensitive KIT Testing Uncovers Previously Undetected KIT Mutations in Patients with Indolent Systemic Mastocytosis: Results from the PIONEER Trial *(Abstract 3164 – Sunday, December 8)*
- Poster Presentation: Disease-Modifying Effects of Avapritinib in Patients with Advanced Systemic Mastocytosis: Improvements in Bone Density *(Abstract 4544 – Monday, December 9)*
- Publication-Only Abstract: Blood-Based Proteomics for Deeper Insights into Indolent Systemic Mastocytosis: the PIONEER Trial Experience *(Abstract 6569)*

About Systemic Mastocytosis

Systemic mastocytosis (SM) is a rare disease driven by the KIT D816V mutation in about 95 percent of cases. Uncontrolled proliferation and activation of mast cells result in chronic, severe and often unpredictable symptoms across multiple organ systems. The vast majority of those affected have indolent systemic mastocytosis (ISM). A broad range of symptoms, including anaphylaxis, maculopapular rash, pruritis, diarrhea, brain fog, fatigue and bone pain, frequently persist in patients with ISM despite treatment with multiple symptom-directed therapies. This burden of disease can lead to a profound, negative impact on quality of life. Patients often live in fear of severe, unexpected symptoms, have limited ability to work or perform daily activities, and isolate themselves to protect against unpredictable triggers. Until 2023, there were no approved therapies for the treatment of ISM.

A minority of patients have advanced SM, which encompasses a group of high-risk SM subtypes including aggressive SM (ASM), SM with an associated hematological neoplasm (SM-AHN) and mast cell leukemia (MCL). In addition to mast cell activation symptoms, advanced SM is associated with organ damage due to mast cell infiltration and poor survival.

About AYVAKIT (avapritinib)

AYVAKIT (avapritinib) is approved by the U.S. Food and Drug Administration (FDA) for the treatment of three indications: adults with ISM, adults with advanced SM, including ASM, SM-AHN and MCL, and adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. Under the brand name AYVAKYT® (avapritinib), this medicine is approved by the European Commission for the treatment of adults with ISM with moderate to severe symptoms inadequately controlled on symptomatic treatment, adults with ASM, SM-AHN and MCL, after at least one systemic therapy, and adults with unresectable or metastatic GIST harboring the PDGFRA D842V mutation. The therapy is not recommended for the treatment of patients with low platelet counts (less than 50,000/µL).

Please click here to see the full U.S. prescribing information for AYVAKIT, and click here to see the European Summary of Product Characteristics for AYVAKYT.

IMPORTANT SAFETY INFORMATION

Intracranial Hemorrhage — Serious intracranial hemorrhage (ICH) may occur with AYVAKIT treatment; fatal events occurred in <1% of patients. Overall, ICH (eg, subdural hematoma, ICH, and cerebral hemorrhage) occurred in 2.9% of 749 patients who received AYVAKIT in clinical trials. In Advanced SM patients who received AYVAKIT at 200 mg daily, ICH occurred in 2 of 75 patients (2.7%) who had platelet counts ≥50 x 10^9/L prior to initiation of therapy and in 3 of 80 patients (3.8%) regardless of platelet counts. In ISM patients, no events of ICH occurred in the 246 patients who received any dose of AYVAKIT in the PIONEER study.

Monitor patients closely for risk factors of ICH which may include history of vascular aneurysm, ICH or cerebrovascular accident within the prior year, concomitant use of anticoagulant drugs, or thrombocytopenia. Symptoms of ICH may include headache, nausea, vomiting, vision changes, or altered mental status. Advise patients to seek immediate medical attention for signs or symptoms of ICH. Permanently discontinue AYVAKIT if ICH of any grade occurs.

In Advanced SM patients, a platelet count must be performed prior to initiating therapy. AYVAKIT is not recommended in Advanced SM patients with platelet counts <50 x 10^9/L. Following treatment initiation, platelet counts must be performed every 2 weeks for the first 8 weeks. After 8 weeks of treatment, monitor platelet counts every 2 weeks or as clinically indicated based on platelet counts. Manage platelet counts of <50 x 10^9/L by treatment interruption or dose reduction.

Cognitive Effects — Cognitive adverse reactions can occur in patients receiving AYVAKIT and occurred in 33% of 995 patients overall in patients who received AYVAKIT in clinical trials including: 28% of 148 Advanced SM patients (3% were Grade ≥3), and 7.8% of patients with ISM who received AYVAKIT + best supportive care (BSC) versus 7.0% of patients who received placebo + BSC (<1% were Grade 3). Depending on the severity and indication, withhold AYVAKIT and then resume at same dose or at a reduced dose upon improvement, or permanently discontinue.

Photosensitivity — AYVAKIT may cause photosensitivity reactions. In all patients treated with AYVAKIT in clinical trials (n=1049), photosensitivity reactions occurred in 2.5% of patients. Advise patients to limit direct ultraviolet exposure during treatment with AYVAKIT and for one week after discontinuation of treatment.

Embryo-Fetal Toxicity — AYVAKIT can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females and males of reproductive potential to use an effective method of contraception during treatment with AYVAKIT and for 6 weeks after the final dose of AYVAKIT. Advise women not to breastfeed during treatment with AYVAKIT and for 2 weeks after the final dose.

Adverse Reactions — The most common adverse reactions (≥20%) in patients with Advanced SM were edema, diarrhea, nausea, and fatigue/asthenia.

The most common adverse reactions (≥10%) in patients with ISM were eye edema, dizziness, peripheral edema, and flushing.

Drug Interactions — Avoid coadministration of AYVAKIT with strong or moderate CYP3A inhibitors. If coadministration with a moderate CYP3A inhibitor cannot be avoided in patients with Advanced SM, reduce dose of AYVAKIT. Avoid coadministration of AYVAKIT with strong or moderate CYP3A inducers. If contraception requires estrogen, limit ethinyl estradiol to ≤20 mcg unless a higher dose is necessary.

To report suspected adverse reactions, contact Blueprint Medicines Corporation at 1-888-258-7768 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

AYVAKIT is available in 25-mg, 50-mg, 100-mg and 200-mg tablets.

Please click here to see the full Prescribing Information for AYVAKIT.

About Blueprint Medicines

Blueprint Medicines is a global, fully integrated biopharmaceutical company that invents life-changing medicines. We seek to alleviate human suffering by solving important medical problems in two core focus areas: allergy/inflammation and oncology/hematology. Our approach begins by targeting the root causes of disease, using deep scientific knowledge in our core focus areas and drug discovery expertise across multiple therapeutic modalities. We have a track record of success with two approved medicines, including AYVAKIT®/AYVAKYT® (avapritinib) which we are bringing to patients with systemic mastocytosis (SM) in the U.S. and Europe.

Leveraging our established research, development, and commercial capability and infrastructure, we now aim to significantly scale our impact by advancing a broad pipeline of programs ranging from early science to advanced clinical trials in mast cell diseases including SM and chronic urticaria, breast cancer and other solid tumors. For more information, visit www.BlueprintMedicines.com and follow us on X (formerly 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 potential benefits of AYVAKIT for the treatment of patients with advanced SM and ISM; statements regarding the HARBOR trial for elenestinib; plans, strategies, timelines and expectations for Blueprint Medicines' current or future approved drugs and drug candidates; the potential benefits of any of Blueprint Medicines' current or future approved drugs or drug candidates in treating patients; and Blueprint Medicines' financial performance, 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," "opportunity," "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 delay of any current or planned clinical trials or the development of the company's current or future drug candidates; the company's 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 possibility that preclinical and clinical results for the company's drug candidates may not support further development of such drug candidates either as monotherapies or in combination with other agents or may impact the anticipated timing of data or regulatory submissions; the timing of the initiation of clinical trials and trial cohorts at clinical trial sites and the possibility patient enrollment rates may be delayed or slower than anticipated; the actions of regulatory agencies and how this may affect the initiation, timing and progress of clinical trials; the company's ability to obtain, maintain and enforce patent and other intellectual property protection for its products and current or future drug candidates it is developing; and the success of the company's 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 the company's 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, the company explicitly disclaims any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements.

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