Blueprint Medicines Announces Positive Top-line Results from PIONEER Trial of AYVAKIT® (avapritinib) in Patients with Non-Advanced Systemic Mastocytosis Achieving Primary and All Key Secondary Endpoints

-- AYVAKIT showed a superior mean change in total symptom score (p=0.003), compared to placebo plus best available care --

-- Highly significant reductions across all objective measures of mast cell burden reinforce the disease modifying activity of AYVAKIT --

-- AYVAKIT had a favorable safety profile compared to the control arm, supporting potential for long-term treatment --

-- Plan to submit supplemental new drug application to FDA in fourth quarter of 2022 --

-- Blueprint Medicines to host investor conference call and webcast today at 8:00 a.m. ET --

CAMBRIDGE, Mass. – August 17, 2022 – Blueprint Medicines Corporation (NASDAQ: BPMC) today announced positive top-line results from the registrational Part 2 of the PIONEER clinical trial of AYVAKIT® (avapritinib) in patients with non-advanced systemic mastocytosis (SM) demonstrating clinically meaningful and highly significant improvements across the primary and all key secondary endpoints, including patient-reported symptoms and objective measures of mast cell burden. Based on these top-line data, Blueprint Medicines plans to submit a supplemental new drug application (sNDA) to the U.S. Food and Drug Administration (FDA) for AYVAKIT in non-advanced SM in the fourth quarter of 2022, with a subsequent submission of a type II variation marketing authorization application to the European Medicines Agency (EMA) anticipated in 2023. In addition, Blueprint Medicines plans to present detailed data from the PIONEER trial at an upcoming medical meeting.

The trial, which was designed to assess AYVAKIT plus best available care versus placebo plus best available care (control arm), achieved its primary endpoint with a highly significant difference in the mean change in total symptom score (TSS) at 24 weeks (p=0.003). TSS was assessed by the Indolent SM Symptom Assessment Form (ISM-SAF). The AYVAKIT arm had a reduction of 15.6 points in mean TSS at 24 weeks, which continued to deepen to 20.2 points at 48 weeks in patients who rolled over to the Part 3 open-label extension study. At 24 weeks, the control arm had a reduction of 9.2 points in mean TSS. In addition, the PIONEER trial met all key secondary endpoints, including significant improvements across all measures of mast cell burden. More than half of AYVAKIT-treated patients had a ≥50 percent reduction of serum tryptase, compared to no patients in the control arm (53.9% vs. 0%; p<0.0001). AYVAKIT was well-tolerated and had a favorable safety profile, and 96.5 percent of AYVAKIT-treated patients completed 24 weeks of therapy, compared to 93.0 percent for the control arm. Overall, 0.7 percent of patients in the AYVAKIT arm and no patients in the control arm discontinued due to treatment-related adverse events.

“As a physician and clinical researcher who has been treating non-advanced systemic mastocytosis patients for over 25 years, I have been awaiting a therapy that decreases the abnormal mast cell burden and activation, improves a wide range of symptoms, and ultimately provides an improved quality of life to patients,” said Mariana Castells, M.D., Ph.D., Director, Mastocytosis Center, Brigham and Women’s Hospital, and an investigator on the PIONEER trial. “For patients with non-advanced SM, PIONEER is the first study to show significant clinical improvements over best available care across patient-reported symptoms and objective measures of disease, with a safety and tolerability profile supporting chronic treatment. The trial results suggest that if approved, AYVAKIT would represent a practice-changing treatment, enabling important clinical benefits for a broad range of patients with non-advanced SM.”

“The PIONEER results showcase Blueprint Medicines’ dedication to advancing the promise of precision therapy for patients with significant medical needs,” said Becker Hewes, M.D., Chief Medical Officer at Blueprint Medicines. “AYVAKIT has the potential to be the first approved medicine for non-advanced SM, and the only treatment that would address the genetic root cause across advanced and non-advanced forms of the disease. Today’s milestone represents a watershed moment for the systemic

mastocytosis community and Blueprint Medicines, capping a decade of collaboration with clinicians, advocates and patients to transform standards of care, and to deepen the understanding of this disease and its impact on various aspects of patients' lives."

AYVAKIT was designed to potently and selectively inhibit D816V mutant KIT, the driver of SM in about 95 percent of cases. SM often leads to debilitating skin, gastrointestinal, neurocognitive and other systemic symptoms, such as life-threatening anaphylaxis.

"Non-advanced systemic mastocytosis is a lifelong disease with severe physical, emotional and social impacts that profoundly reduce patients' quality of life," said Lauren Denton, Executive Director of The Mast Cell Disease Society. "Patients with SM continue to be challenged by efforts to avoid various triggers of everyday life while also managing complex therapies. The PIONEER clinical trial results offer hope to these patients and help pave the way for new innovation in treatment."

"These new data are the culmination of a dedicated long-term collaboration and shared 'patients first' core value between Blueprint Medicines and The Mast Cell Disease Society. We are excited by these results and further energized to work together with these exceptional investigators to transform the lives of patients, offering them a better quality of life and the gift of time," said Valerie Slee, Board Chair of The Mast Cell Disease Society.

Top-line Data from the PIONEER Trial

Part 2 of the registrational PIONEER trial was designed to evaluate the efficacy and safety of AYVAKIT (25 mg once-daily dosing; N=141) versus control (N=71) over 24 weeks of treatment. Eligibility criteria include an indolent SM diagnosis confirmed by central pathology review, and moderate-to-severe symptom burden despite an optimized regimen of best available care. Patients were able to continue symptom-directed therapies while receiving AYVAKIT or placebo. Results were reported as of a data cutoff date of June 23, 2022.

Baseline data, including mean TSS, were consistent with Part 1 of the trial. The PIONEER study achieved its primary endpoint and all key secondary endpoints, with AYVAKIT showing highly significant improvements in patient-reported symptoms and objective measures of disease burden.

Clinical Outcome Measures: AYVAKIT Arm vs. Control Arm		P-value[a]
Primary Endpoint	Mean Change in TSS	p=0.003
Secondary Endpoints[b]	≥30% Reduction in Mean TSS	p=0.009
	≥50% Reduction in Mean TSS	p=0.005
	Mean Change in Most Severe Symptom Score	p=0.015
	≥50% Reduction in Serum Tryptase	p<0.0001
	≥50% Reduction in KIT D816V Variant Allele Fraction	p<0.0001
	≥50% Reduction in Bone Marrow Mast Cell Aggregates	p<0.0001

[a] One-sided p-value <0.025 indicates statistical significance.
[b] For secondary endpoints, reductions in TSS and objective measures of mast cell burden represent proportion of patients with ≥30% and ≥50% reductions. All endpoints are key secondary endpoints, except for mean change in most severe symptom score, which is an additional secondary endpoint.

AYVAKIT had a favorable safety profile compared to the control arm. The rate of adverse events (AEs) was 90.8 percent in the AYVAKIT arm and 93.0 percent in the control arm. Serious AEs occurred in 5.0 percent of AYVAKIT-treated patients, compared to 11.3 percent of patients in the control arm. Discontinuations due to treatment-related AEs occurred in 0.7 percent of AYVAKIT-treated patients and 0 percent of patients in the placebo arm. The AYVAKIT arm had a lower rate of cognitive AEs than the

control arm (2.8% AYVAKIT vs. 4.2% control), and there were no intracranial bleeding events. Treatment-related AEs reported in at least three patients in either arm and at least 5 percent of AYVAKIT-treated patients included headache (7.8% AYVAKIT vs. 9.9% control), nausea (6.4% AYVAKIT vs 8.5% control), peripheral edema (6.4% AYVAKIT vs. 1.4% control) and periorbital edema (6.4% AYVAKIT vs. 2.8% control). In the AYVAKIT arm, 93.0 percent of edema AEs were Grade 1 and the remainder were Grade 2.

Conference Call Information

Blueprint Medicines will host a live conference call and webcast at 8:00 a.m. ET today to discuss the top-line data from the PIONEER trial. The conference call may be accessed by dialing 844-200-6205 (domestic) or 929-526-1599 (international), and referring to conference ID 806215. A webcast of the call will also be available under "Events and Presentations" in the Investors & Media section of the Blueprint Medicines website at http://ir.blueprintmedicines.com/. The archived webcast will be available on the Blueprint Medicines website approximately two hours after the conference call and will be available for 30 days following the call.

About AYVAKIT (avapritinib)

AYVAKIT (avapritinib) is a kinase inhibitor approved by the FDA for the treatment of adults with Advanced SM, including aggressive SM (ASM), SM with an associated hematological neoplasm (SM-AHN) and mast cell leukemia (MCL), and adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. For more information, visit AYVAKIT.com. This medicine is approved in Europe (AYVAKYT®) for the treatment of adults with ASM, SM-AHN or MCL, after at least one systemic therapy, and adults with unresectable or metastatic GIST harboring the PDGFRA D842V mutation. 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.

AYVAKIT/AYVAKYT is not approved for the treatment of any other indication in the U.S. or Europe. The FDA granted breakthrough therapy designation to AYVAKIT for the treatment of moderate to severe indolent SM.

To learn about ongoing or planned clinical trials, contact Blueprint Medicines at medinfo@blueprintmedicines.com or 1-888-BLU-PRNT (1-888-258-7768). Additional information is available at blueprintclinicaltrials.com or clinicaltrials.gov.

About Systemic Mastocytosis

Systemic mastocytosis (SM) is a rare disease primarily driven by the KIT D816V mutation. Uncontrolled proliferation and activation of mast cells result in chronic, severe and often unpredictable symptoms for patients across the spectrum of SM. The vast majority of those affected have non-advanced (indolent or smoldering) SM, with debilitating symptoms that lead to a profound, negative impact on quality of life. A minority of patients have advanced SM, which encompasses a group of high-risk SM subtypes including ASM, SM-AHN and MCL. In addition to mast cell activation symptoms, advanced SM is associated with organ damage due to mast cell infiltration and poor survival. Across advanced SM subtypes, the median overall survival is approximately 3.5 years in ASM, approximately two years in SM-AHN and less than six months in MCL.

Debilitating symptoms, including anaphylaxis, maculopapular rash, pruritis, diarrhea, brain fog, fatigue and bone pain, often persist across all forms of SM despite treatment with a number of symptom-directed therapies. 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. Historically, there had been no approved therapies for the treatment of SM that selectively inhibit D816V mutant KIT.

About the PIONEER Trial

PIONEER is a randomized, double-blind, placebo-controlled, registrational trial evaluating AYVAKIT in patients with non-advanced SM. The trial includes three parts: dose-finding Part 1, registrational Part 2 and long-term treatment Part 3. Key trial endpoints include the change in patient-reported disease symptoms as measured by the ISM-SAF TSS, patient-reported quality of life, quantitative measures of mast cell burden and safety. Patients who completed Part 1 or 2 were eligible to participate in Part 3. All patients receive AYVAKIT treatment during Part 3, including those rolling over from the control arm. For more information about the PIONEER trial, please visit www.clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT03731260).

About Blueprint Medicines

Blueprint Medicines is a global precision therapy company that invents life-changing therapies for people with cancer and blood disorders. Applying an approach that is both precise and agile, we create medicines 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 approved medicines directly to patients in the United States and Europe, and we are globally advancing multiple programs for systemic mastocytosis, lung cancer and other genomically defined cancers, 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 plans to submit a supplemental new drug application (sNDA) to the U.S. Food and Drug Administration (FDA) for AYVAKIT in patients with non-advanced SM, with a subsequent submission of a type II variation marketing authorization application to the European Medicines Agency (EMA), plans and timing for presenting detailed data from the PIONEER trial of AYVAKIT in patients with non-advanced SM, and expectations regarding the potential benefits of AYVAKIT in treating patients with non-advanced SM. 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 continuing to establish and expand a commercial infrastructure, and successfully launching, marketing and selling current or future approved products; Blueprint Medicines’ ability to successfully expand the approved indications for AYVAKIT/AYVAKYT or obtain marketing approval for AYVAKIT/AYVAKYT 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 or of an approved product in an additional indication 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 either as monotherapies or in combination with other agents or may impact the anticipated timing of data or regulatory submissions; the risk that “topline” data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to

confirmation, audit, and verification procedures that could result in material changes in the final data; the timing of the initiation of clinical trials and trial cohorts at clinical trial sites and patient enrollment rates; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; Blueprint Medicines' ability to obtain, maintain and enforce patent and other intellectual property protection for AYVAKIT/AYVAKYT; Blueprint Medicines' ability to develop and commercialize companion diagnostic tests for AYVAKIT/AYVAKYT; Blueprint Medicines' ability to successfully expand its operations, research platform and portfolio of therapeutic candidates, and the timing and costs thereof; and the success of Blueprint Medicines' current and future collaborations, financing arrangements, 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.

Trademarks

Blueprint Medicines, AYVAKIT, AYVAKYT and associated logos are trademarks of Blueprint Medicines Corporation.

Investor Relations Contact

Jenna Cohen
+1 (857) 209-3147
ir@blueprintmedicines.com

Media Relations Contact

Andrew Law
+1 (617) 844-8205
media@blueprintmedicines.com