



FDA Approves AYVAKIT® (avapritinib) as the First and Only Treatment for Indolent Systemic Mastocytosis

-- For the first time, patients with indolent SM have a medicine that treats the primary disease driver and is proven to provide broad and durable symptom relief --

-- Approval based on the positive PIONEER trial, in which once-daily AYVAKIT achieved significant improvements in disease symptoms and measures of mast cell burden, with a safety profile that compared favorably to placebo --

-- Blueprint Medicines to host investor conference call and webcast today at 4:30 p.m. ET --

CAMBRIDGE, Mass., May 22, 2023 -- Blueprint Medicines Corporation (Nasdaq: BPMC) today announced that the U.S. Food and Drug Administration (FDA) has approved [AYVAKIT](#)® (avapritinib) for the treatment of adults with indolent systemic mastocytosis (ISM). All U.S. patients with ISM now have access to the first and only approved medicine designed to treat their disease.

Systemic mastocytosis (SM) is a rare hematologic disorder that can lead to a range of debilitating symptoms across multiple organ systems and a significant impact on patients' quality of life. ISM represents the vast majority of SM cases, and AYVAKIT is now available for adults with ISM at the recommended dose of 25 mg once daily. AYVAKIT was designed to potently and selectively inhibit KIT D816V, the primary underlying driver of the disease. AYVAKIT has been FDA approved for the treatment of advanced SM since June 2021.

"Today's approval of AYVAKIT reflects more than a decade of collaboration and leadership in the field of systemic mastocytosis, during which our team at Blueprint Medicines has worked closely with clinicians, patients and their families, and patient advocacy groups to advance innovative science and develop a transformational treatment for people living with the disease," said Becker Hewes, M.D., Chief Medical Officer at Blueprint Medicines. "AYVAKIT is the first and only medicine approved by the FDA to treat indolent systemic mastocytosis, marking a shift in the treatment paradigm from supportive care to disease modifying therapy. In addition, AYVAKIT is the only treatment approved across the spectrum of indolent and advanced systemic mastocytosis. With a broad indication for indolent systemic mastocytosis and a strong label, we are now engaging healthcare providers to redefine what it means for their patients to be well-controlled as well as activating the patient community to seek out optimal care and treatment."

"After decades of caring for people with indolent systemic mastocytosis, I have seen firsthand its profound impact on patients' underlying mast cell burden, symptoms, physical and mental health, and ability to work and participate in daily activities," said Cem Akin, M.D., Ph.D., Professor of Medicine at the University of Michigan,¹ and an investigator on the PIONEER trial.¹ "Despite the use of multiple supportive care treatments, a considerable number of patients with indolent systemic mastocytosis continue to experience a substantial disease burden. AYVAKIT advances the treatment of indolent systemic mastocytosis by targeting KIT D816V, the primary underlying cause of the disease, and establishes a new standard of care for a broad population of patients with this disorder. AYVAKIT delivered statistically significant and consistent clinical improvements in the PIONEER trial, and based on these practice-changing data, I feel a tremendous sense of hope for the future for all those affected by the disease."

The approval of AYVAKIT in ISM is based on data from the double-blind, placebo-controlled PIONEER trial – the largest study ever conducted for this disease – in which patients received AYVAKIT 25 mg once daily plus best supportive care (AYVAKIT) or placebo plus best supportive care (placebo). AYVAKIT demonstrated significant improvements versus placebo in the primary and all key secondary endpoints, including overall symptoms and measures of mast cell burden.

AYVAKIT was well-tolerated with a favorable safety profile compared to placebo, and most adverse reactions were mild to moderate in severity. The most common adverse reactions for AYVAKIT (≥10 percent) were eye edema, dizziness, peripheral edema and flushing. Serious adverse reactions and discontinuations due to adverse reactions occurred in less than 1 percent of patients.

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Detailed results from the PIONEER trial, including open-label extension study data showing the clinical benefits of AYVAKIT through 48 weeks of treatment, were presented in February 2023 at the American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting.

“People with indolent systemic mastocytosis are significantly impacted by their disease symptoms, and many individuals self-isolate at home to protect against unpredictable external triggers. Ultimately, the disease can disrupt an individual’s quality of life, career and ability to interact with family and friends, and those affected often face frequent healthcare visits and significant polypharmacy burden,” said Judith Kain Emmel, Board Chair of The Mast Cell Disease Society. “Since we began nearly 30 years ago, our goals as an organization have been to educate, advocate and collaborate for the advancement of knowledge and research in mast cell disorders like systemic mastocytosis. Today’s approval is a historic moment for the SM community and offers new hope for patients and their families. We are honored to have contributed to this milestone by facilitating SM community insights on the design of the PIONEER trial and supporting the development of the validated symptom assessment tool used in the study.”

Blueprint Medicines is committed to patient access and affordability for its approved medicines through YourBlueprint®, which is designed to provide dedicated, personalized assistance for eligible patients. Commercially insured patients who qualify for the company’s co-pay assistance program may pay as little as \$0 in out-of-pocket costs for AYVAKIT. YourBlueprint offers additional programs intended to facilitate timely access to therapy, including a patient assistance program for eligible patients who have inadequate insurance coverage. For more information, visit [YourBlueprint.com](https://yourblueprint.com) or call 1-888-BLUPRNT (1-888-258-7768), Monday to Friday, 8:00 a.m. to 8:00 p.m. ET. Healthcare providers who prescribe AYVAKIT can fill out an enrollment form at [YourBlueprint.com/HCP](https://yourblueprint.com/HCP) to help patients access Blueprint Medicines’ support programs.

Investor Conference Call Information

Blueprint Medicines will host a live conference call and webcast today at 4:30 p.m. ET to discuss the FDA approval of AYVAKIT in ISM. The conference call may be accessed by dialing 833-470-1428 (domestic) or 404-975-4839 (international), and referring to conference ID 832860. A webcast of the call will also be available under “Events and Presentations” in the Investors & Media section of the Blueprint Medicines website at <https://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 precision therapy approved by the FDA for the treatment of three indications: adults with ISM, 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](https://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 [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.

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

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

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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. Historically, there had been 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 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.

Important Safety Information

Intracranial Hemorrhage—Serious intracranial hemorrhage (ICH) may occur with AYWAKIT 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 AYWAKIT in clinical trials. In Advanced SM patients who received AYWAKIT at 200 mg daily, ICH occurred in 2 of 75 patients (2.7%) who had platelet counts $\geq 50 \times 10^9/L$ 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 AYWAKIT 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 AYWAKIT if ICH of any grade occurs. In Advanced SM patients, a platelet count must be performed prior to initiating therapy. AYWAKIT is not recommended in Advanced SM patients with platelet counts $< 50 \times 10^9/L$. 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 $< 50 \times 10^9/L$ by treatment interruption or dose reduction.

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

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

Embryo-Fetal Toxicity—AYWAKIT 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 AYWAKIT and for 6 weeks after the final dose of AYWAKIT. Advise women not to breastfeed during treatment with AYWAKIT and for 2 weeks after the final dose.

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

The most common adverse reactions ($\geq 10\%$) 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.

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

Please click here to see the full [Prescribing Information](#) for AYVAKIT.

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 our approved medicines to patients in the United States and Europe, and we are globally advancing multiple programs for systemic mastocytosis, lung cancer, breast 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 Blueprint Medicines' views with respect to the FDA approval of AYVAKIT/AYVAKYT and the implications of such approval for patients, caregivers and healthcare professionals; expectations regarding patients' ability to rapidly access treatment with AYVAKIT/AYVAKYT; Blueprint Medicines' plans and ability to provide robust support services for patients prescribed AYVAKIT/AYVAKYT through YourBlueprint; the potential benefits of Blueprint Medicines' current and future approved drugs or drug candidates in treating patients, including expectations regarding the potential of AYVAKIT/AYVAKYT to address additional tumor types and treatment settings; 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 our ability and plans in continuing to expand Blueprint Medicines' 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 our 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 either as monotherapies or in combination with other agents or may impact the anticipated timing of data or regulatory submissions; 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 its products or any drug candidates it is developing; Blueprint Medicines' ability to develop and commercialize companion diagnostic tests for its products or any of its current and future drug candidates; Blueprint Medicines' ability to successfully expand its research platform and the costs thereof; 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 its Annual Report on Form 10-K for the year ended December 31, 2022, as filed with the SEC on February 16, 2023, and any other filings that Blueprint Medicines has made or may make with the SEC in

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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 assumes no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

Reference

¹ Title provided for identification purposes only. The views and opinions expressed are those of the individual only and do not necessarily reflect the positions of the University of Michigan. Dr. Akin has a paid consulting/advisory relationship with Blueprint Medicines Corporation.

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