



FDA Approves Blueprint Medicines' AYVAKIT™ (avapritinib) for the Treatment of Adults with Advanced Systemic Mastocytosis

-- First precision therapy that specifically targets the primary driver of the disease --

-- Durable clinical responses, including complete remissions, shown in patients with or without prior treatment --

-- Full approval supported by robust efficacy and safety data from two clinical trials --

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

CAMBRIDGE, Mass., June 16, 2021 – Blueprint Medicines Corporation (NASDAQ: BPMC) today announced that the U.S. Food and Drug Administration (FDA) has approved [AYVAKIT™](#) (avapritinib) for the treatment of adult patients with advanced systemic mastocytosis (Advanced SM), including aggressive SM (ASM), SM with an associated hematological neoplasm (SM-AHN) and mast cell leukemia (MCL). For the first time, advanced SM patients can now receive a targeted therapy designed to potently and selectively inhibit D816V mutant KIT, the central driver of the disease.

“Today’s approval of AYVAKIT for advanced systemic mastocytosis – the fourth FDA approval across our portfolio in 18 months – culminates nearly a decade of hard work, from our scientists in the laboratory and clinical team conducting trials, to our commercial organization who will now bring AYVAKIT to patients,” said Jeff Albers, Chief Executive Officer of Blueprint Medicines. “As shown in two clinical trials, AYVAKIT provides remarkable clinical efficacy to patients with advanced systemic mastocytosis, and this approval solidifies the therapy’s strong value proposition in this population. With a deep commitment to driving continued research innovation in collaboration with the mast cell disease community, we are now building on this progress with the goal of bringing the benefits of precision therapy to a broader range of patients through our ongoing and planned clinical trials for non-advanced systemic mastocytosis.”

SM is a rare hematologic disorder caused by the KIT D816V mutation in nearly all cases. 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.¹

“Advanced systemic mastocytosis is a debilitating disease characterized by extensive damage in multiple organ systems due to mast cell infiltration, and new treatment options are urgently needed to address these life-threatening complications,” said Daniel DeAngelo, M.D., Ph.D., Chief of the Division of Leukemia at Dana-Farber Cancer Institute. “Avapritinib will clearly establish a new standard of care for patients with advanced systemic mastocytosis. The FDA approval was based on data showing robust and durable responses, including complete remissions, and a favorable safety profile. For advanced SM patients, the approval of avapritinib shifts the treatment paradigm toward precision therapy that targets the primary driver of mastocytosis.”

The FDA granted full approval to AYVAKIT for adults with advanced SM based on data from the Phase 1 EXPLORER trial and Phase 2 PATHFINDER trial.² Treatment response was evaluated using modified IWG-MRT-ECNM criteria, with assessments based on at least 12 weeks of response duration, resolution of at least one finding of non-hematologic and hematologic organ damage, and 50 percent or greater reductions in biomarker response, mast cell burden and serum tryptase. The overall response rate (ORR) in the U.S. prescribing information is defined as complete remission with full or partial hematologic recovery (CR/CRh), or partial remission (PR).

AYVAKIT showed durable clinical efficacy in advanced SM patients across disease subtypes and regardless of prior therapy. In 53 evaluable patients who had a median follow-up of 11.6 months, the ORR was 57 percent (95% CI: 42%, 70%), and the proportion of patients with CR/CRh (28 percent), PR (28 percent) and clinical improvement (15 percent) is in line with previously reported results. The median duration of response was 38.3 months (95% CI: 19 months, not estimable). Warnings and precautions include intracranial hemorrhage, cognitive effects and embryo-fetal toxicity. AYVAKIT is not recommended for the treatment of patients with advanced SM with low platelet counts (less than 50,000/ μ L), which is consistent with current patient eligibility criteria in the EXPLORER and PATHFINDER trials. The most common adverse reactions were edema, diarrhea, nausea and fatigue/asthenia.

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“People with advanced systemic mastocytosis face a scary, uncertain future due to life-threatening complications of the disease, as well as debilitating symptoms that often profoundly alter their ability to perform daily activities, and the FDA approval of a new therapy, AYVAKIT, brings much needed hope to these patients,” said Valerie Slee, Board Chair of The Mast Cell Disease Society.

“This milestone is also the culmination of many years of work across the systemic mastocytosis community, and we’re proud of the contributions The Mast Cell Disease Society has made to improve the understanding of this disease, pioneer new approaches to measuring the impact of therapeutic interventions, and support the development of important medicines like AYVAKIT,” said Lauren Denton, Executive Director of The Mast Cell Disease Society. “We look forward to continuing our collaboration with Blueprint Medicines, scientific and clinical experts, and other stakeholders across our community to improve diagnosis, treatment and care for all patients living with systemic mastocytosis.”

Blueprint Medicines is committed to advancing precision therapies for the benefit of SM patients. The company is developing AYVAKIT for the treatment of non-advanced SM patients, and BLU-263, a next-generation KIT D816V inhibitor, to further address the range of medical needs in this patient population.

For advanced SM patients receiving AYVAKIT, Blueprint Medicines provides access and affordability programs through YourBlueprint™. For more information, visit 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 to help patients access Blueprint Medicines’ support programs.

The recommended dose of AYVAKIT in advanced SM is 200 mg once daily. AYVAKIT is available in 200 mg, 100 mg, 50 mg and 25 mg dose strengths for advanced SM patients.

Conference Call Information

Blueprint Medicines will host a live webcast beginning at 4:30 p.m. ET today to discuss the FDA approval of AYVAKIT in advanced SM. To access the live call, please dial (833) 921-1639 (domestic) or (236) 389-2650 (international) and refer to conference ID 4328214. 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 90 days following the call.

About AYVAKIT (avapritinib)

AYVAKIT (avapritinib) is a kinase inhibitor approved by the FDA for the treatment of two indications: adults with Advanced SM, including ASM, SM-AHN and MCL, and adults with unresectable or metastatic gastrointestinal stromal tumors (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 unresectable or metastatic GIST harboring the PDGFRA D842V mutation, and in Mainland China (AYVAKIT®) for the treatment of adults with unresectable or metastatic PDGFRA exon 18 mutant GIST.

AYVAKIT/AYVAKYT is not approved for the treatment of any other indication in the U.S., Europe or Greater China, or for any indication in any other jurisdiction by any other health authority.

Blueprint Medicines is developing AYVAKIT globally for the treatment of advanced and non-advanced SM. The FDA granted breakthrough therapy designation to AYVAKIT for the treatment of advanced SM, including the subtypes of ASM, SM-AHN and MCL, and 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-BLUPRNT (1-888-258-7768). Additional information is available at pioneertrial.com or clinicaltrials.gov.

Blueprint Medicines has an exclusive collaboration and license agreement with CStone Pharmaceuticals for the development and commercialization of AYVAKIT in Mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains development and commercial rights for AYVAKIT in the rest of the world.

About SM

SM is a rare disease 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.

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 symptomatic 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.

Important Safety Information

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 Advanced SM patients who received AYVAKIT 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. Monitor patients closely for risk of ICH including those with thrombocytopenia, vascular aneurysm or a history of ICH or cerebrovascular accident within the prior year. Permanently discontinue AYVAKIT if ICH of any grade occurs. A platelet count must be performed prior to initiating therapy. AYVAKIT 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 adverse reactions can occur in patients receiving AYVAKIT. Cognitive adverse reactions occurred in 39% of 749 patients and in 28% of 148 SM patients (3% were Grade > 3). Memory impairment occurred in 16% of patients; all events were Grade 1 or 2. Cognitive disorder occurred in 10% of patients; <1% of these events were Grade 3. Confusional state occurred in 6% of patients; <1% of these events were Grade 3. Other events occurred in <2% of patients. Depending on the severity, withhold AYVAKIT and then resume at same dose or at a reduced dose upon improvement, or permanently discontinue.

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.

The most common adverse reactions ($\geq 20\%$) at all doses were edema, diarrhea, nausea, and fatigue/asthenia.

Avoid coadministration of AYVAKIT with strong and moderate CYP3A inhibitors. If coadministration with a moderate CYP3A inhibitor cannot be avoided, reduce dose of AYVAKIT. Avoid coadministration of AYVAKIT with strong and 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 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 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 Blueprint Medicines' views with respect to the approval of AYVAKIT and the implications of such approval for patients, caregivers and healthcare professionals; expectations concerning when additional dose strengths of AYVAKIT will be commercially available in the U.S.; Blueprint Medicines' plans and ability to provide support programs for patients prescribed AYVAKIT 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 and BLU-263 to address non-advanced SM; and Blueprint Medicines' strategy, goals and anticipated milestones, business plans and focus. The words "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 maintain 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 (avapritinib) and GAVRETO® (pralsetinib) 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 obtain, maintain and enforce patent and other intellectual property protection for AYVAKIT/AYVAKYT, GAVRETO or any drug candidates it is developing; Blueprint Medicines' ability to develop and commercialize companion diagnostic tests for AYVAKIT/AYVAKYT, GAVRETO or any of 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.

References

¹ Sperr WR, Kundi M, Alvarez-Twose I, et al. International prognostic scoring system for mastocytosis (IPSM): a retrospective cohort study. *Lancet Haematol*. 2019;6(12):e638-e649.

² AYVAKIT™ (avapritinib) Prescribing Information (U.S.). Blueprint Medicines Corporation, Cambridge, Massachusetts, USA; June 2021.

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