Blueprint Medicines, a Sanofi Company, Highlights Long-Term Clinical Benefit of AYVAKIT® (avapritinib) Across Indolent and Advanced Systemic Mastocytosis at 2025 ASH Annual Meeting

-- Durable disease control and quality-of-life improvements for patients with ISM in the PIONEER trial --

-- Prolonged survival, including in the first-line treatment setting, for patients with advanced SM in the PATHFINDER trial --

CAMBRIDGE, Mass., December 5, 2025 -- Blueprint Medicines, a Sanofi company, today announced updated data reinforcing the clinical efficacy and safety of long-term AYVAKIT® (avapritinib) use across the spectrum of systemic mastocytosis (SM), including indolent and advanced SM. AYVAKIT led to sustained symptom and quality-of-life benefits in indolent SM (ISM) after a median follow-up of more than three years, and extended survival rates in advanced SM after a median follow-up of more than four years. Across both forms of SM, AYVAKIT showed bone health improvements reflecting disease-modifying effects, and a safety and tolerability profile consistent with previously reported results. As part of its ongoing leadership to improve SM care, Blueprint Medicines will report one oral presentation and seven poster presentations at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition, December 6–9 in Orlando, Florida.

“Our ASH data add to the substantial body of evidence generated since we initiated clinical development for systemic mastocytosis about a decade ago, and reflect the transformative benefits AYVAKIT has delivered since its FDA approval for advanced SM in 2021 and ISM in 2023,” said Mik Rinne, M.D., Ph.D., Head of Development at Blueprint Medicines. “AYVAKIT has become the global standard of care across the spectrum of the disease, with robust datasets highlighting sustained quality-of-life benefits in ISM, favorable survival outcomes in advanced SM and a well-characterized safety profile supporting chronic treatment. Our presentations reinforce the urgency to treat the root cause of SM to mitigate its significant health complications and underscore the role of AYVAKIT as a best-in-class therapy for the long-term management of the disease.”

PIONEER: Durable Symptom Control, Quality-of-Life Benefits and Bone Health Improvements in ISM, with a Multi-Year Safety Profile Similar to the 24-Week Placebo-Controlled Portion of the Trial (Poster Presentations; Abstract Numbers 2024, 5582)

- In patients with ISM (N=226), AYVAKIT showed sustained improvements in overall symptoms, all symptom domains (skin, gastrointestinal, neurocognitive) and most severe symptom per the ISM Symptom Assessment Form (ISM-SAF), and in quality of life per the Mastocytosis Quality of Life Questionnaire (MC-QoL).
- AYVAKIT led to durable benefits in bone health among patients receiving dual-energy X-ray absorptiometry (DXA) scans (n=79), independent of concomitant use of other treatments known to improve bone density.
- With a median follow-up of more than three years, the overall trial population had a 3 percent discontinuation rate due to treatment-related adverse events (TRAEs), reflecting a best-in-class safety and tolerability profile. Edema was the most common TRAE, and the majority of these events were mild (Grade 1).

PATHFINDER: Prolonged Survival, Robust Clinical Responses and Improved Bone Health with a Consistent Safety Profile Over Time in Advanced SM (Oral Presentation; Abstract Number 1022)

- In patients with advanced SM receiving first-line AYVAKIT (n=38), the median overall survival (OS) was not reached and the OS rate at 48 months was 79 percent after a median follow-up of more than four years, reflecting sustained clinical benefit.
- Historically, advanced SM has been associated with poor survival.[1,2] In a prior clinical trial of midostaurin, the median OS was 28.7 months for patients with advanced SM.[1]

Blueprint Medicines, a Sanofi company
45 Sidney Street
Cambridge, MA 02139
+1 (617) 374-7580

- In treatment-naïve patients who were response evaluable (n=30), the overall response rate (ORR) was 87 percent, and the rate of complete remissions with full or partial hematologic recovery (CR/CRh) was 43 percent.
- Among patients receiving DXA scans across lines of therapy (n=56), 21 percent had low bone density at baseline. In this population, AYVAKIT significantly increased bone density versus baseline levels ($p<0.05$).
- In patients across lines of therapy (N=107), AYVAKIT had a favorable benefit/risk profile consistent with previously reported data. Common TRAEs were edema (periorbital and peripheral), thrombocytopenia and anemia.

PATHFINDER: Survival Benefits in Intermediate- and High-Risk Patients with Advanced SM, a Historically Underserved Population (Poster Presentation; Abstract Number 5595)

- This analysis included patients with advanced SM who had intermediate- and high-risk prognostic scores at baseline, as determined by the Mutation-Adjusted Risk Score (MARS).
- In the treatment-naïve setting, PATHFINDER results for AYVAKIT (n=24) were indirectly compared to real-world data for midostaurin (n=43), and statistical methods were used to adjust for baseline demographic differences between the two patient populations.
- AYVAKIT was associated with improved OS relative to midostaurin (Hazard Ratio [HR]: 0.08; $p<0.001$) in these patients, who have traditionally had the worst prognosis.

Data Presentations

- Oral Presentation: Avapritinib Treatment of Patients with Advanced Systemic Mastocytosis: 4-Year Safety, Effect on Bone and First-Line Efficacy Results of the PATHFINDER Clinical Study *(Abstract #1022 – Monday, December 8)*
- Poster Presentation: Avapritinib Achieves Deep and Durable Symptom Control with a Well-Tolerated Safety Profile in ISM: Long-Term Outcomes from PIONEER *(Abstract #2024 – Saturday, December 6)*
- Poster Presentation: Effect of Avapritinib on Skin Lesions in Patients with Advanced Systemic Mastocytosis Using a Novel, Artificial Intelligence-Based Technology (PATHFINDER) *(Abstract #2030 – Saturday, December 6)*
- Poster Presentation: Changes in Long-Term Bone Health in Patients Receiving Avapritinib for the Treatment of Indolent Systemic Mastocytosis in the PIONEER Study *(Abstract #5582 – Monday, December 8)*
- Poster Presentation: Improved Overall Survival in Patients with Advanced Systemic Mastocytosis Treated with Avapritinib Versus Real-World Therapy Based on Mutation-Adjusted Risk Score (MARS) Stratification *(Abstract #5595 – Monday, December 8)*
- Poster Presentation: An Analysis of Clonal Dynamics in Patients with Indolent Systemic Mastocytosis Treated with Avapritinib in the PIONEER Study *(Abstract #5573 – Monday, December 8)*
- Poster Presentation: Diagnostic Evolution in Systemic Mastocytosis: Clinical Impact of WHO 2022 Criteria on Smoldering Systemic Mastocytosis Identification in PIONEER *(Abstract #5578 – Monday, December 8)*
- Poster Presentation: Interpreting Tryptase Levels and Avoiding Common Pitfalls in Screening for Clonal Mast Cell Disease *(Abstract #4774 – Monday, December 8)*

At the start of its oral session and at 8:00 a.m. ET on the day of their respective poster sessions, data presentations will be available in the "Science—Publications and Presentations" section of Blueprint Medicines' website, www.blueprintmedicines.com.

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). Despite treatment with multiple symptom-directed therapies, patients with ISM frequently experience persistent symptoms including anaphylaxis, maculopapular rash, pruritus, diarrhea, brain fog, fatigue and bone pain, as well as long-term health complications such as osteoporosis. 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. There were no approved therapies for ISM until 2023, when AYVAKIT received U.S. Food and Drug Administration (FDA) approval for this indication.

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 – including bone lesions, malabsorption, liver dysfunction and bone marrow failure – as well as poor overall survival.

About Blueprint Medicines' Clinical Trials in SM

Blueprint Medicines has pursued a broad clinical development program for patients living with SM, including three registrational trials for AYVAKIT and one for elenestinib. PIONEER is a randomized, double-blind, placebo-controlled trial designed to assess the safety and clinical efficacy of AYVAKIT in patients with ISM, and PATHFINDER and EXPLORER are open-label, single-arm trials designed to evaluate the safety and clinical efficacy of AYVAKIT in patients with advanced SM.

The HARBOR trial of elenestinib, an investigational next-generation KIT D816V inhibitor, is currently enrolling patients with ISM. HARBOR is a randomized, double-blind, placebo-controlled study that includes dose-finding Part 1, registrational Part 2 and long-term treatment Part 3. All patients who complete Parts 1 or 2 have an opportunity to receive treatment with elenestinib in Part 3. Key trial endpoints include changes in patient-reported symptoms, biomarkers and bone mineral density, annualized rate of anaphylaxis events, and safety.

Patients and clinicians interested in the ongoing HARBOR trial can contact Blueprint Medicines at medinfo@blueprintmedicines.com or +1 (617) 714-6707. Additional details are available at https://clinicaltrials.gov/study/NCT04910685 or https://harborclinicaltrial.com.

About AYVAKIT

AYVAKIT (avapritinib) is the first and only medicine approved by the FDA to treat the root cause of SM. It was FDA approved for the treatment of advanced SM in June 2021 and ISM in May 2023. It now is indicated in 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. The medicine is approved in the EU as AYVAKYT® for the treatment of adults with ISM with moderate to severe symptoms inadequately controlled on symptomatic treatment, 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. The therapy is not recommended for the treatment of patients with low platelet

counts (less than 50,000/μL). Globally, the medicine is approved for one or more indications in more than 35 countries worldwide, including China where it has been developed and commercialized by CStone Pharmaceuticals, which pays tiered percentage royalties on sales.

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 U.S. Prescribing Information for AYVAKIT.

About Blueprint Medicines, a Sanofi Company

Blueprint Medicines, a Sanofi company, seeks to alleviate human suffering by solving important medical problems in allergy/inflammation and oncology/hematology. Our approach begins by targeting the root causes of disease, leveraging deep expertise in our core focus areas. We have a track record of success with two approved medicines, including AYVAKIT/AYVAKYT (avapritinib) which we are bringing to patients with SM in the U.S. and Europe, and we aim to scale our impact by advancing programs in mast cell diseases and solid tumors. For more information, visit www.blueprintmedicines.com and follow us on X (formerly Twitter; @BlueprintMeds) and LinkedIn.

Footnotes

[1] Gotlib J, Kluin-Nelemans, HC, George TI, et al. Efficacy and Safety of Midostaurin in Advanced Systemic Mastocytosis. *N Engl J Med*. 2016;374:2530–2541.

[2] 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.

Trademarks

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

Media Contact

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