Blueprint Medicines, a Sanofi Company, Announces Four-Year PIONEER Data Showing Sustained Benefit and Long-Term Safety of AYVAKIT® (avapritinib) in Indolent Systemic Mastocytosis

-- Real-world study of AYVAKIT highlights improvement across ISM symptoms --

-- 12 data presentations at 2026 AAAAI Annual Meeting reflect company's leadership in elevating SM care --

CAMBRIDGE, Mass., February 28, 2026 -- Blueprint Medicines, a Sanofi company, today announced AYVAKIT® (avapritinib) data showing clinically meaningful outcomes and a well-tolerated long-term safety profile in patients with indolent systemic mastocytosis (ISM). Key presentations include four-year PIONEER clinical study results highlighting sustained symptom control and quality of life improvement in AYVAKIT-treated patients, and real-world data showing meaningful symptom benefit in patients receiving the therapy in a community practice setting. In addition, a study conducted with the Advanced Practitioner Society for Hematology and Oncology (APSHO) and The Mast Cell Disease Society (TMS) reinforces the severe symptoms and impaired quality of life experienced by patients with ISM. In total, 12 data presentations are being reported at the 2026 American Academy of Allergy, Asthma and Immunology (AAAAI) Annual Meeting, February 27 – March 2 in Philadelphia.

"Patients with indolent systemic mastocytosis and healthcare providers have expressed the need for a therapy that meaningfully improves quality of life through durable symptom benefit and a safety profile enabling long-term treatment, and AYVAKIT is delivering this significant impact to a wide range of people living with the disease," said Mik Rinne, M.D., Ph.D., Head of Development at Blueprint Medicines. "Across clinical and real-world settings, AYVAKIT has shown robust efficacy and a well-tolerated safety profile, helping patients realize the sustained benefit of KIT D816V-targeted therapy. In addition, emerging evidence continues to underscore the substantial burden of SM, highlighting the urgency to treat the underlying cause of the disease."

PIONEER: Long-Term Data Reinforce AYVAKIT as Durable Standard of Care in ISM
Abstracts 509, 518, 530

- Patients showed continued improvement through four years in overall symptoms, all symptom domains (skin, gastrointestinal [GI], neurocognitive) and most severe symptom per the ISM Symptom Assessment Form (ISM-SAF), and quality of life per the Mastocytosis Quality of Life Questionnaire (MC-QoL).
- In patients with frequent episodes of diarrhea at baseline and at least four years of AYVAKIT (n=44), the median reduction in diarrhea frequency was 65.6 percent. In the overall clinical study population, individual GI symptoms meaningfully improved, allowing for decreased use of cromolyn sodium and other supportive care medicines.
- Patients had increased bone mineral density – a clinical measure of disease-modifying effects – in the lumbar spine, left total hip and left femoral neck after three years of AYVAKIT. In PIONEER, the change in bone mineral density was assessed in patients who received dual-energy X-ray absorptiometry (DXA) scans (n=79).
- With a median patient follow-up of about four years (46.5 months; N=226), the safety of AYVAKIT was consistent with the 24-week placebo-controlled portion of the clinical study, and the discontinuation rate due to treatment-related adverse events (TRAEs) was 3 percent (n=6). The majority of edema events, the most common TRAEs, were mild (Grade 1).

Real-World Evidence Further Validates Clinical Benefit of AYVAKIT in ISM
Abstracts 516, 529

- A retrospective review of electronic medical records was conducted at ONCare Alliance, a network of community oncology practices, to assess the impact of AYVAKIT in the real-world setting. Median follow-up was 14.2 months.
- In AYVAKIT-treated patients (N=18), the median time to symptom improvement was rapid (36.5 days). Benefits were frequently reported across a range of symptoms, including GI, skin, abdominal pain and headache symptoms.
- Among patients who initiated the 25 mg daily dose of AYVAKIT (n=16), 87.5 percent have remained on therapy, reflecting a well-tolerated safety profile.
- An additional presentation features a systematic literature review of AYVAKIT data, including results from the real-world AVATAR study in patients with uncontrolled ISM (N=17). In this study, the median MC-QoL score decreased from 61 (baseline) to 17 (24 weeks), representing a 76 percent improvement.

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Lack of Disease Control and Substantial Burden in Patients with ISM
Abstract 514

- In collaboration with APSHO and TMS, a survey was developed to identify factors affecting perceptions of disease control in patients with ISM (N=53).
- Three-quarters of patients (75 percent; n=40) reported that their disease was not optimally controlled.
- Patients reported severe symptoms regardless of their perceived disease control, underscoring the significant burden across the spectrum of ISM.

Copies of the AAAAI poster presentations are available in the "Science—Publications and Presentations" section of Blueprint Medicines' website, www.blueprintmedicines.com.

- Avapritinib Continues to Demonstrate Durable Symptom Control with a Well-Tolerated Safety Profile: Long-Term Outcomes from PIONEER *(Abstract 509 – Saturday, February 28)*
- Real-World Experience of Patients with Indolent Systemic Mastocytosis Treated with Avapritinib in a Community Oncology Setting *(Abstract 516 – Saturday, February 28)*
- Avapritinib Durably Improves Gastrointestinal Symptoms of Indolent Systemic Mastocytosis: Long-Term Outcomes from the PIONEER Study *(Abstract 518 – Saturday, February 28)*
- Long-Term Bone Health Outcomes in Patients Treated with Avapritinib for Indolent Systemic Mastocytosis: Findings from the PIONEER Study *(Abstract 530 – Saturday, February 28)*
- A Systematic Literature Review of Avapritinib Outcomes in Indolent Systemic Mastocytosis (ISM) Patients *(Abstract 529 – Saturday, February 28)*
- Understanding Disease Control: What Shapes Patient Experience in Indolent Systemic Mastocytosis *(Abstract 514 – Saturday, February 28)*
- When One Is Diagnosed, Two Are Changed: The Caregiver Experience in Indolent Systemic Mastocytosis *(Abstract 513 – Saturday, February 28)*
- Systemic Mastocytosis: Five-Year Mortality Comparison with Matched Reference Cohorts *(Abstract 533 – Saturday, February 28)*
- Mortality Risk by Subtype in Systemic Mastocytosis: A Retrospective Cohort Analysis *(Abstract 522 – Saturday, February 28)*
- Ultra-Sensitive SuperRCA Assay Enhances the Ability to Detect KIT D816V Mutations in Peripheral Blood with a Sensitivity Comparable to That of Bone Marrow Testing *(Abstract 524 – Saturday, February 28)*
- Are Tryptase Thresholds for Systemic Mastocytosis Adequate? Electronic Health Record (EHR) Data Weigh In *(Abstract 527 – Saturday, February 28)*
- Project BEACON: Developing a Predictive Model to Accelerate Diagnosis of Indolent Systemic Mastocytosis *(Abstract 517 – Saturday, February 28)*

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 Studies in SM

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

The HARBOR clinical study (NCT04910685) of elenestinib, an investigational next-generation KIT D816V inhibitor, is currently enrolling patients with ISM. HARBOR is a randomized, double-blind, placebo-controlled clinical 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 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 clinical study 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

Cognitive Effects — Cognitive adverse reactions can occur in patients receiving AYVAKIT and occurred in 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, withhold AYVAKIT and then resume at the same dose, or permanently discontinue AYVAKIT.

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 contraception during treatment with AYVAKIT and for 6 weeks after the final dose. Advise women not to breastfeed during treatment with AYVAKIT and for 2 weeks following the final dose.

Adverse Reactions — 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 or 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 visit www.fda.gov/medwatch.

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.

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