



**Blueprint Medicines Announces FDA Approval of AYWAKIT™ (avapritinib) for the Treatment of Adults with Unresectable or Metastatic PDGFRA Exon 18 Mutant Gastrointestinal Stromal Tumor**

-- AYWAKIT is the first approved precision therapy for GIST and the only highly active treatment for PDGFRA exon 18 mutant GIST --

-- AYWAKIT showed an 84% overall response rate and a median duration of response was not reached in patients with unresectable or metastatic PDGFRA exon 18 mutant GIST in the NAVIGATOR trial<sup>1</sup> --

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

CAMBRIDGE, Mass., January 9, 2020 – Blueprint Medicines Corporation (NASDAQ: BPMC), a precision therapy company focused on genomically defined cancers, rare diseases and cancer immunotherapy, today announced that the U.S. Food and Drug Administration (FDA) has approved [AYVAKIT™](#) (avapritinib) for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations. AYWAKIT is the first precision therapy approved to treat a genomically defined population of patients with GIST.

The FDA granted a full approval to AYWAKIT based on efficacy results from the Phase 1 NAVIGATOR clinical trial, as well as combined safety results from multiple clinical trials for avapritinib. In patients with PDGFRA exon 18 mutant GIST, AYWAKIT had an overall response rate (ORR) of 84 percent (95% CI: 69%, 93%), and a median duration of response (DOR) was not reached. The most common adverse reactions (≥20 percent) were edema, nausea, fatigue/asthenia, cognitive impairment, vomiting, decreased appetite, diarrhea, hair color changes, increased lacrimation, abdominal pain, constipation, rash and dizziness. Blueprint Medicines plans to make AYWAKIT available in the U.S. within a week.

GIST is a rare, genomically driven sarcoma of the gastrointestinal (GI) tract. Approximately 6 percent of patients with newly diagnosed GIST have PDGFRA exon 18 mutations. The most common PDGFRA exon 18 mutation is the D842V mutation, which is resistant to all other approved therapies. A retrospective study showed that when these patients were treated with imatinib, they had an ORR of 0 percent.<sup>2</sup>

“Today’s approval of AYWAKIT brings forward a new standard of care for patients with PDGFRA exon 18 mutant GIST, a genomically defined population that previously had very limited treatment options. For the first time, we can offer these patients a highly effective treatment that targets the underlying genetic cause of their disease,” said Michael Heinrich, M.D., Professor of Medicine at Oregon Health & Science University and an investigator on the NAVIGATOR trial. “Building on our growing understanding of the molecular basis of GIST, this milestone ushers in a new era of precision medicine in this disease. The FDA approval represents a call to action to conduct mutational testing in all patients with GIST before initiating kinase inhibitor therapy, as recommended by clinical guidelines, so appropriate patients may realize the benefits of this promising new medicine.”

“The full approval of AYWAKIT based on robust data from our Phase 1 NAVIGATOR clinical trial is an incredibly exciting milestone for our company and, more importantly, for GIST patients with a PDGFRA exon 18 mutation, who have been waiting for a new treatment option,” said Jeff Albers, Chief Executive Officer at Blueprint Medicines. “AYVAKIT is the first of what we hope will be many approved medicines enabled by our research platform. Now, as we begin to deliver AYWAKIT to patients and their healthcare providers, we aim to fortify our leadership in the field of precision medicine and build a foundation for our broader portfolio by pairing our strong research and development capabilities with an equally talented commercial organization focused on addressing patient needs, accelerating diagnostic testing and enabling access.”

Blueprint Medicines is dedicated to helping patients with PDGFRA exon 18 mutant GIST access treatment with AYWAKIT and providing robust support throughout their treatment journey. As part of this commitment, Blueprint Medicines is introducing YourBlueprint™, a patient support program that offers access and affordability solutions for individuals receiving AYWAKIT. 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 AYWAKIT can fill out an enrollment form at [YourBlueprint.com/HCP](#) to help patients access Blueprint Medicines’ support services.

#### Conference Call Information

Blueprint Medicines will host a live webcast beginning at 4:30 p.m. ET today to discuss the FDA approval of AYWAKIT. To access the live call, please dial (855) 728-4793 (domestic) or (503) 343-6666 (international), and refer to conference ID 5579052. A webcast of the conference call will be available 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.

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## Update on New Drug Application for the Treatment of Fourth-Line GIST

Blueprint Medicines today announced that the FDA administratively split the proposed indications for avapritinib under the initial New Drug Application (NDA) into two separate NDAs: one for PDGFRA exon 18 mutant GIST, which the FDA approved today, and one for fourth-line GIST. The Prescription Drug User Fee Act (PDUFA) action date for the fourth-line GIST indication is currently February 14, 2020. As previously announced, for the NDA for fourth-line GIST an extension of up to three months for the PDUFA action date will likely be required to enable Blueprint Medicines to provide top-line data to the FDA from VOYAGER, a Phase 3 clinical trial evaluating avapritinib versus regorafenib in third- or fourth-line GIST.

### AYVAKIT Efficacy and Safety Data<sup>1</sup>

The efficacy of AYVAKIT was established from 43 patients in the NAVIGATOR trial with unresectable or metastatic GIST harboring PDGFRA exon 18 mutations, including 38 patients with PDGFRA D842V mutations. These patients were treated at starting doses of either 300 mg once daily (QD) or 400 mg QD. Efficacy data were evaluated by blinded, independent central radiology review, based on modified Response Evaluation Criteria in Solid Tumors version 1.1 (mRECIST 1.1 criteria) for GIST. The recommended dose of AYVAKIT is 300 mg QD. AYVAKIT is available in 100 mg, 200 mg and 300 mg dose strengths.

AYVAKIT demonstrated durable responses in patients with PDGFRA exon 18 mutations across multiple lines of treatment. In these patients, the ORR was 84 percent [7 percent complete responses (CR), 77 percent partial responses (PR)]. In patients with PDGFRA D842V mutations, the ORR was 89 percent (95% CI: 75%, 97%; 8 percent CR, 82 percent PR). The median DOR was not reached in either patient population (range: 1.9+ months, 20.3+ months).

The safety of AYVAKIT in patients with unresectable or metastatic GIST was evaluated in 204 patients who received 300 mg QD or 400 mg QD dosing in the NAVIGATOR trial. Patients were heavily pre-treated, with patients receiving a median of three prior kinase inhibitors (range: 0 to 7).

There are no contraindications for AYVAKIT. AYVAKIT has warnings and precautions of intracranial hemorrhage, central nervous system effects and embryo-fetal toxicity. The most common adverse reactions (≥20 percent) were edema, nausea, fatigue/asthenia, cognitive impairment, vomiting, decreased appetite, diarrhea, hair color changes, increased lacrimation, abdominal pain, constipation, rash and dizziness.

### About AYVAKIT (avapritinib)

AYVAKIT (avapritinib) is a kinase inhibitor approved by the FDA for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. AYVAKIT is a selective and potent inhibitor of KIT and PDGFRA mutant kinases. It is the only FDA-approved type 1 inhibitor for GIST that works by directly binding to the active kinase conformation from which mutant KIT and PDGFRA signal. AYVAKIT has demonstrated inhibition of a broad range of KIT and PDGFRA mutations associated with GIST, including potent clinical activity against activation loop mutations that are associated with resistance to currently approved therapies. For more information, visit [AYVAKIT.com](https://www.blueprintmed.com/AYVAKIT.com).

Avapritinib is not approved for the treatment of any other indication in the U.S. or any other jurisdiction by the FDA or any other health authority.

Blueprint Medicines is pursuing a broad clinical development program for avapritinib across multiple lines of GIST treatment, as well as for advanced, smoldering and indolent systemic mastocytosis (SM). The FDA has granted Breakthrough Therapy Designation to avapritinib for two indications: one for the treatment of unresectable or metastatic GIST harboring the PDGFRA D842V mutation and one for the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia. For more information about avapritinib clinical trials, visit [www.clinicaltrials.gov](https://www.clinicaltrials.gov) or [www.blueprintclinicaltrials.com](https://www.blueprintclinicaltrials.com).

### About GIST

GIST is a sarcoma, or tumor of bone or connective tissue, of the GI tract. Tumors arise from cells in the wall of the GI tract and occur most often in the stomach or small intestine. Most patients are diagnosed between the ages of 50 to 80, and diagnosis is typically triggered by GI bleeding, incidental findings during surgery or imaging and, in rare cases, tumor rupture or GI obstruction.

Most GIST cases are caused by mutations in KIT or PDGFRA that force protein kinases into an increasingly active state. Because other available therapies primarily bind to the inactive protein conformations, certain primary and secondary mutations typically result in treatment resistance and lead to disease progression.

In unresectable or metastatic GIST, clinical benefits from existing treatments can vary by mutation type. Mutational testing is critical to tailor therapy to the underlying disease driver and is recommended in expert guidelines. Currently, there are no approved therapies for patients with KIT-driven GIST whose disease progresses beyond imatinib, sunitinib and regorafenib. In patients with advanced PDGFRA D842V-driven GIST treated with imatinib, a retrospective study showed an ORR of 0 percent.<sup>2</sup>

### **Important Safety Information**

Intracranial hemorrhage (e.g., subdural hematoma, intracranial hemorrhage, and cerebral hemorrhage) occurred in 1% of 267 patients (0.7% Grade 3 or 4) with GIST and overall in 3% of 335 patients (1.2% Grade 3 or 4) who received AYVAKIT. Overall, 0.9% of patients receiving AYVAKIT required permanent discontinuation for an intracranial hemorrhage. Withhold AYVAKIT and then resume at a reduced dose upon resolution, or permanently discontinue AYVAKIT based on severity.

In 335 patients receiving AYVAKIT, CNS adverse reactions occurred overall in 58% of patients including cognitive impairment (41%; 3.6% Grade 3 or 4), dizziness (20%; 0.6% Grade 3 or 4), sleep disorders (15%; 0.3% Grade 3 or 4), mood disorders (13%; 1.5% Grade 3 or 4), speech disorders (6%; none Grade 3 or 4), and hallucinations (2.1%; none Grade 3 or 4). Overall, 3.9% of patients required permanent discontinuation of AYVAKIT for a CNS adverse reaction. Depending on severity, withhold AYVAKIT and then resume at the same dose or at a reduced dose upon improvement, or permanently discontinue AYVAKIT.

AYVAKIT can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential and 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 two weeks after the final dose. Advise females and males of reproductive potential that AYVAKIT may impair fertility.

In 204 patients with unresectable or metastatic GIST, the most common adverse reactions ( $\geq 20\%$ ) were edema, nausea, fatigue/asthenia, cognitive impairment, vomiting, decreased appetite, diarrhea, hair color changes, increased lacrimation, abdominal pain, constipation, rash and dizziness.

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.

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

### **About Blueprint Medicines**

Blueprint Medicines is a precision therapy company striving to improve human health. With a focus on genomically defined cancers, rare diseases and cancer immunotherapy, we are developing transformational medicines rooted in our leading expertise in protein kinases, which are proven drivers of disease. Our uniquely targeted, scalable approach empowers the rapid design and development of new treatments and increases the likelihood of clinical success. We have one FDA-approved precision therapy and are currently advancing multiple investigational medicines in clinical development, along with a number of research programs. For more information, visit [www.BlueprintMedicines.com](http://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 AYVAKIT will be commercially available in the U.S.; Blueprint Medicines' plans and ability to provide robust support services for patients prescribed AYVAKIT through YourBlueprint; plans, timelines and expectations for interactions with the FDA and other regulatory authorities; plans, timelines and expectations related to the NDA for fourth-line GIST and any extension of the PDUFA action date; 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 Blueprint Medicines' ability and plan in establishing a commercial infrastructure, and successfully launching, marketing and selling its approved product; Blueprint Medicines' ability to successfully expand the indication for AYVAKIT in the future; the delay of any current or planned clinical trials or the development of Blueprint Medicines' drug candidates or licensed product candidate; 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 develop and commercialize companion diagnostic tests for its current and future drug candidates; and the success of Blueprint Medicines' current and future collaborations or licensing arrangements, including its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., its collaboration with CStone Pharmaceuticals and its license to Clementia Pharmaceuticals. 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 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

<sup>1</sup> AYVAKIT™ (avapritinib) Prescribing Information (U.S.). Blueprint Medicines Corporation, Cambridge, Massachusetts, USA; January 2020.

<sup>2</sup> Cassier PA, Fumagalli E, Rutkowski P., et al. Outcome of patients with platelet-derived growth factor receptor alpha-mutated gastrointestinal stromal tumors in the tyrosine kinase inhibitor era. *Clin Cancer Res.* 2012;18(16):4458-4464.

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