



Blueprint Medicines Announces Initial Data from Phase 2 PIONEER Trial of Avapritinib in Patients with Indolent Systemic Mastocytosis Showing Activity at All Dose Levels Tested

- Plan to initiate screening in registration-enabling portion of PIONEER trial in indolent SM in first half 2020 --
- Top-line EXPLORER trial data in advanced SM support planned NDA submission in Q1 2020 --
- Blueprint Medicines to host investor event and webcast on Sunday, December 8, 2019 at 8:30 p.m. ET --

CAMBRIDGE, Mass., December 8, 2019 – Blueprint Medicines Corporation (NASDAQ:BPMC), a precision therapy company focused on genomically defined cancers, rare diseases and cancer immunotherapy, today announced initial data from the Phase 2 PIONEER clinical trial of avapritinib in patients with indolent systemic mastocytosis (SM). Initial data from the dose-finding Part 1 of the PIONEER trial showed rapid and robust reductions in serum tryptase, a well-established measure of mast cell burden, in patients treated with 25 mg, 50 mg or 100 mg of avapritinib once daily (QD). All dose levels of avapritinib tested were well-tolerated, and no patients discontinued treatment due to an adverse event (AE). The results will be presented today in a poster presentation at the 61st American Society of Hematology (ASH) Annual Meeting and Exposition in Orlando, Florida.

Nearly all cases of SM, a rare mast cell disorder, are driven by the KIT D816V mutation, which aberrantly activates mast cells. Patients across all disease subtypes including indolent SM experience debilitating symptoms across multiple organ systems, while advanced SM is uniquely characterized by organ damage due to mast cell infiltration. Avapritinib, an investigational drug, is a highly potent and selective inhibitor of D816V mutant KIT.

“Patients with indolent SM often experience debilitating symptoms, including unpredictable hypersensitivity reactions and anaphylaxis, despite available symptom-directed treatments, leading to reduced quality of life, social isolation and frequent utilization of the healthcare system,” said Cem Akin, M.D., Ph.D., Professor of Medicine at the University of Michigan and an investigator on the PIONEER trial. “The initial PIONEER data announced today are highly encouraging and show that low doses of avapritinib are well-tolerated and reduce elevated levels of tryptase in the blood. We believe this early indicator of mast cell response is predictive of reductions in clinical symptoms, which we hope to see confirmed with additional data from the PIONEER trial next year.”

“The PIONEER data in patients with indolent SM further highlight the potential of avapritinib, a highly potent inhibitor of D816V mutant KIT, to become a new standard of care across all subtypes of SM,” said Andy Boral, M.D., Ph.D., Chief Medical Officer at Blueprint Medicines. “Blueprint Medicines is committed to advancing a comprehensive clinical development program for avapritinib, with the goal of bringing a highly effective precision therapy to a broad population of patients with SM.”

Blueprint Medicines plans to report additional data from Part 1 of the PIONEER trial that will inform the selection of a recommended Part 2 dose (RP2D), including the change in patient-reported disease symptoms as measured by the Indolent SM Symptom Assessment Form (ISM-SAF), in the first quarter of 2020. The registration-enabling Part 2 of the PIONEER trial is anticipated to initiate patient screening in the first half of 2020.

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Highlights from the ASH Presentation of PIONEER Trial Data in Indolent SM

The dose-finding Part 1 of the PIONEER trial was designed to test three doses of avapritinib (25 mg, 50 mg and 100 mg QD) versus placebo to determine a RP2D. Major eligibility criteria included adults with indolent SM confirmed by central pathology review and moderate to severe symptom burden, despite best available supportive care medications. Across four concurrent cohorts, 39 patients were enrolled, including 10 patients in each avapritinib dose cohort and nine patients in the placebo cohort. As of a data cutoff date of November 12, 2019, the enrolled population had a median time on study of 12 weeks (range: 1-30 weeks).

Baseline Patient Characteristics

At baseline, all patients had symptomatic disease despite best available therapy. Median ISM-SAF total symptom score (TSS) was 52 [range: 19-100 (total possible range: 0-110)]. Patients were taking a median of three medications (range: 1-7) to treat their disease. Mean serum tryptase was 84 micrograms per liter.

Clinical Activity Data

Across all avapritinib dose cohorts, reductions in serum tryptase were robust, occurred rapidly and were sustained in patients treated up to 30 weeks. The placebo cohort showed no change in serum tryptase at 12 weeks.

Mean Percent Change in Serum Tryptase				
Timepoint	Avapritinib 25 mg QD	Avapritinib 50 mg QD	Avapritinib 100 mg QD	Placebo
Cycle 1, Day 8 (first post-baseline assessment)	-37.72%	-54.08%	-56.16%	7.05%
Cycle 4, Day 1 (12 weeks)	-48.24%	-66.67%	-61.83%	0.39%

Tryptase is an enzyme released by activated mast cells. Elevated tryptase in blood serum is a hallmark of SM and a component of the World Health Organization diagnostic criteria. Reduction in serum tryptase is a component of the IWG-MRT-ECNM response criteria (IWG criteria) for advanced SM.

Safety Data

All doses of avapritinib tested were well-tolerated, and most reported AEs were Grade 1 or 2. There were no reported cases of intracranial bleeding, thrombocytopenia or anemia. Across all avapritinib cohorts, five patients (16.7 percent) had Grade 3 AEs, and no patients had serious AEs. In patients treated with placebo, two patients (22.2 percent) had Grade 3 AEs, and two patients (22.2 percent) had serious AEs. There was one Grade 3 cognitive effect reported in the 100 mg cohort. The event resolved following dose modification, and the patient remained on therapy as of the data cutoff date. No patients discontinued treatment due to an AE.



Top-line EXPLORER Trial Data and NDA Submission Plan for Avapritinib in Advanced SM

Blueprint Medicines plans to submit a new drug application (NDA) to the U.S. Food and Drug Administration (FDA) for avapritinib for the treatment of patients with advanced SM in the first quarter of 2020. The planned NDA will include response data for approximately 55 patients and safety data for approximately 100 patients from the EXPLORER trial and the PATHFINDER trial.

Blueprint Medicines today announced top-line results from the EXPLORER trial. The company plans to report top-line data from the PATHFINDER trial in the first quarter of 2020 and expects these data will be generally consistent with the top-line EXPLORER data.

As of a data cutoff of August 30, 2019, top-line efficacy data from the EXPLORER trial showed a centrally confirmed overall response rate (ORR) of 77 percent in 48 patients evaluable for response per the modified IWG criteria. ORR was defined as complete remission with full or partial recovery of peripheral blood counts, partial remission or clinical improvement. Median duration of response (DOR) and median overall survival were not reached. Median follow-up was 21 months, with patients receiving ongoing treatment up to approximately 3.5 years.

The top-line safety results were generally consistent with previously reported data. In 80 patients evaluable for safety as of the data cutoff date, avapritinib was generally well-tolerated with most AEs reported by investigators as Grade 1 or 2. Across all grades, the most common treatment-emergent AEs reported by investigators were periorbital edema, anemia, diarrhea, fatigue, peripheral edema, nausea, thrombocytopenia, vomiting and cognitive effects. Only six patients discontinued due to treatment-related adverse events.

As of the data cutoff date, no new intracranial bleeding events had been observed in the EXPLORER trial since the company previously presented data at the 24th Congress of the European Hematology Association. After the data cutoff date, one patient with SM and an associated hematologic neoplasm (SM-AHN) of myelodysplastic syndrome had a Grade 5 intracranial bleed. At the time of the bleeding event, the patient had severe thrombocytopenia and experienced a serious injury involving head trauma.

Investor Event and Webcast Information

Blueprint Medicines will host an investor event on Sunday, December 8, 2019 beginning at 8:30 p.m. ET in Orlando to review initial data from the PIONEER trial. The event will be webcast live and can be accessed under "Events and Presentations" in the Investors & Media section of Blueprint Medicines' website at <http://ir.blueprintmedicines.com>. A replay of the webcast will be available approximately two hours after the event and will be available for 30 days following the event.

About the Clinical Development Program for Avapritinib in SM

Blueprint Medicines is pursuing a broad clinical development program for avapritinib across advanced, indolent and smoldering forms of SM. Avapritinib is currently being evaluated in three ongoing, registration-enabling clinical trials for SM: the EXPLORER trial, the PATHFINDER trial and the PIONEER trial.

The EXPLORER trial is an open-label, single-arm trial designed to identify the RP2D and demonstrate proof-of-concept in patients with advanced SM. Key trial endpoints include ORR, DOR, quantitative measures of mast cell burden, patient-reported outcomes and safety. The EXPLORER trial has completed patient enrollment.



The PATHFINDER trial is an open-label, single-arm registration-enabling trial designed to confirm the clinical activity of avapritinib in approximately 60 patients with advanced SM. Key trial endpoints include ORR, DOR, quantitative measures of mast cell burden, patient-reported outcomes and safety. Patient enrollment is ongoing at sites in the United States, Canada and European Union.

The PIONEER trial is a randomized, double-blind, placebo-controlled, registration-enabling trial in approximately 112 patients with indolent and smoldering SM. The trial includes three parts: dose-finding Part 1, registration-enabling Part 2 and long-term treatment Part 3. All patients who complete Parts 1 or 2 will have an opportunity to continue to receive treatment with avapritinib in Part 3. Key trial endpoints include the change in patient-reported disease symptoms as measured by the ISM-SAF TSS, quantitative measures of mast cell burden and safety. Part 1 has completed patient enrollment. Part 2 is anticipated to initiate patient screening in the first half of 2020 at sites in the United States, Canada and European Union.

SM patients and clinicians interested in ongoing or planned clinical trials can contact the Blueprint Medicines study director at studydirector@blueprintmedicines.com or 1-617-714-6707. Additional details are available at www.pathfindertrial.com, www.pioneertrial.com or www.clinicaltrials.gov.

About SM

SM is one disease driven by the KIT D816V mutation. The majority of patients have indolent SM with symptoms that range from burdensome to life-threatening. A minority of patients have advanced SM, which encompasses a group of high-risk SM subtypes, including aggressive SM (ASM), SM-AHN and mast cell leukemia (MCL), which are associated with organ damage due to mast cell infiltration and poor overall survival. In nearly all SM patients, the KIT D816V mutation aberrantly activates mast cells. Aberrant mast cell activation and proliferation results in chronic, severe and often unpredictable symptoms, such as pruritus, flushing, headaches, bone pain, nausea, vomiting, diarrhea, anaphylaxis, abdominal pain and fatigue. Currently, there are no approved therapies that selectively inhibit D816V mutant KIT.

About Avapritinib

Avapritinib is an investigational, oral precision therapy that selectively and potently inhibits KIT and PDGFRA mutant kinases. It is a type 1 inhibitor designed to target the active kinase conformation; all oncogenic kinases signal via this conformation. Avapritinib has demonstrated broad inhibition of KIT and PDGFRA mutations associated with gastrointestinal stromal tumors (GIST), including potent activity against activation loop mutations that are associated with resistance to currently approved therapies.

Blueprint Medicines is initially developing avapritinib for the treatment of advanced GIST, advanced SM, and indolent and smoldering 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.

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



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 are currently advancing three investigational medicines in clinical development, along with multiple research programs. For more information, visit www.BlueprintMedicines.com and follow us on [Twitter](https://twitter.com/BlueprintMeds) (@BlueprintMeds) and [LinkedIn](https://www.linkedin.com/company/blueprint-medicines).

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 plans and timelines for the development of its drug candidates, including the timing, design, implementation, enrollment, plans and announcement of results regarding Blueprint Medicines' ongoing and planned clinical trials for avapritinib and BLU-263; plans, timelines and expectations for additional data from Part 1 of the PIONEER trial and for initiating patient screening in Part 2 of the PIONEER trial; plans, timelines and expectations for top-line PATHFINDER trial data; plans, timelines and expectations for interactions with the FDA and other regulatory authorities; plans and timelines for submitting an NDA to the FDA for avapritinib for the treatment of advanced SM; expectations regarding the potential benefits of avapritinib treating patients with 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 delay of any current or planned clinical trials or the development of Blueprint Medicines' drug candidates, including avapritinib, pralsetinib, fisogatinib and BLU-263, or licensed products, including BLU-782; 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.



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