UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): **December 8, 2019**

Blueprint Medicines Corporation
(Exact name of registrant as specified in its charter)

Delaware	**001-37359**	**26-3632015**
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

45 Sidney Street **Cambridge, Massachusetts**	**02139**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(617) 374-7580**

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common stock, par value $0.001 per share	BPMC	Nasdaq Global Select Market

Item 7.01 Regulation FD Disclosure.

On December 8, 2019, Blueprint Medicines Corporation (the "Company") issued a press release announcing initial data from the dose-finding portion (part 1) of its ongoing Phase 2 PIONEER clinical trial in patients with indolent systemic mastocytosis and top-line data from its Phase 1 EXPLORER clinical trial evaluating avapritinib for the treatment of advanced systemic mastocytosis. The PIONEER trial data were presented on Sunday, December 8, 2019 in a poster presentation at the 61st American Society of Hematology Annual Meeting and Exposition ("ASH Annual Meeting") in Orlando, Florida. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K, and a copy of the presentation at the ASH Annual Meeting is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

In addition, on December 8, 2019, the Company hosted an investor event and live webcast to discuss the data presented at the ASH Annual Meeting. A copy of the presentation from the investor event is furnished as Exhibit 99.3 to this Current Report on Form 8-K.

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.1, 99.2 and 99.3, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press release issued by Blueprint Medicines Corporation on December 8, 2019
99.2	Presentation by Blueprint Medicines Corporation at the ASH Annual Meeting on December 8, 2019
99.3	Presentation by Blueprint Medicines Corporation at the investor event on December 8, 2019
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

BLUEPRINT MEDICINES CORPORATION

Date: December 9, 2019

By: /s/ Jeffrey W. Albers
Jeffrey W. Albers
Chief Executive Officer

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.

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 (@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 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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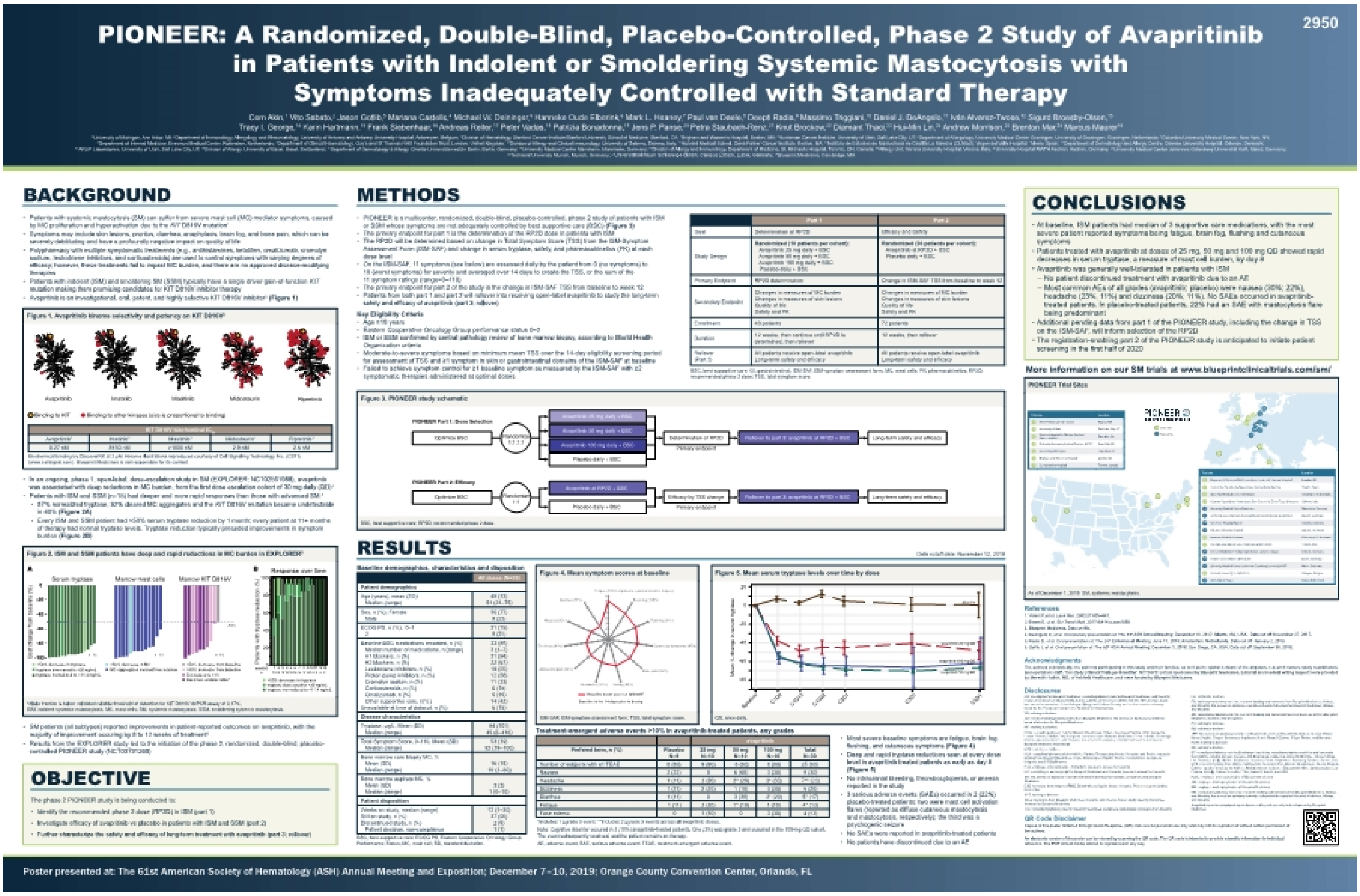
Exhibit 99.2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PIONEER: A Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study of Avapritinib in Patients with Indolent or Smoldering Systemic Mastocytosis with Symptoms Inadequately Controlled with Standard Therapy
BACKGROUND
METHODS
CONCLUSIONS
RESULTS
OBJECTIVE
More information on our SM trials at www.blueprintclinicaltrials.com/sm/
Poster presented at: The 61st American Society of Hematology (ASH) Annual Meeting and Exposition; December 7–10, 2019; Orange County Convention Center, Orlando, FL

Systemic Mastocytosis Program Update

ASH 2019 ANNUAL MEETING

DECEMBER 8, 2019

blueprint™ MEDICINES

Forward-looking statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. 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. In this presentation, forward-looking statements include, without limitation, statements regarding plans and timelines for the development of avapritinib, pralsetinib, fisogatinib, and BLU-263, including the timing, design, implementation, enrollment, plans and announcement of results or data for ongoing and planned clinical trials for the drug candidates of Blueprint Medicines Corporation (the "Company"); plans and timelines for current and future marketing applications for avapritinib and pralsetinib; the potential benefits of the Company's current and future drug candidates in treating patients; and the Company's strategy, goals and anticipated milestones, business plans and focus. The Company has based these forward-looking statements on management's current expectations, assumptions, estimates and projections. While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks, uncertainties and other important factors, many of which are beyond the Company's control and may cause actual results, performance or achievements to differ materially from those expressed or implied by any forward-looking statements. These risks and uncertainties include, without limitation, risks and uncertainties related to the delay of any current or planned clinical trials or the development of the Company's drug candidates, including avapritinib, pralsetinib, fisogatinib and BLU-263, or the licensed products, including BLU-782; the Company's advancement of multiple early-stage efforts; the Company's ability to successfully demonstrate the efficacy and safety of its drug candidates and gain approval of its drug candidates on a timely basis, if at all; the preclinical and clinical results for the Company's drug candidates, which may not support further development of such drug candidates; actions or decisions of regulatory agencies or authorities, which may affect the initiation, timing and progress of clinical trials; the Company's ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing; the Company's ability to develop and commercialize companion diagnostic tests for its current and future drug candidates; and the success of the Company's current and future collaborations, partnerships, or licenses, including its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, "Roche"), its collaboration with CStone Pharmaceuticals ("CStone") and its license agreement with Clementia Pharmaceuticals Inc. ("Clementia").

These and other risks and uncertainties are described in greater detail under "Risk Factors" in the Company's filings with the Securities and Exchange Commission ("SEC"), including the Company's most recent Quarterly Report on Form 10-Q and any other filings the Company has made or may make with the SEC in the future. The Company cannot guarantee future results, outcomes, levels of activity, performance, developments, or achievements, and there can be no assurance that the Company's expectations, intentions, anticipations, beliefs, or projections will result or be achieved or accomplished. The forward-looking statements in this presentation are made only as of December 8, 2019, and except as required by law, the Company undertakes no obligation to update any forward-looking statements contained in this presentation as a result of new information, future events or otherwise.

This presentation also contains estimates, projections and other statistical data made by independent parties and by the Company relating to market size and growth and other data about the Company's industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of the Company's future performance and the future performance of the markets in which the Company operates are necessarily subject to a high degree of uncertainty and risk.

Agenda

Welcome	**Jeff Albers** Chief Executive Officer
Initial PIONEER trial data for avapritinib in indolent SM	**Daniel DeAngelo, MD, PhD** Director, Clinical and Translational Research, Adult Leukemia, Dana-Farber Cancer Institute Associate Professor of Medicine, Harvard Medical School
SM development program update	**Andy Boral, MD, PhD** Chief Medical Officer
Questions and answers	**All**
Closing remarks	**Jeff Albers** Chief Executive Officer

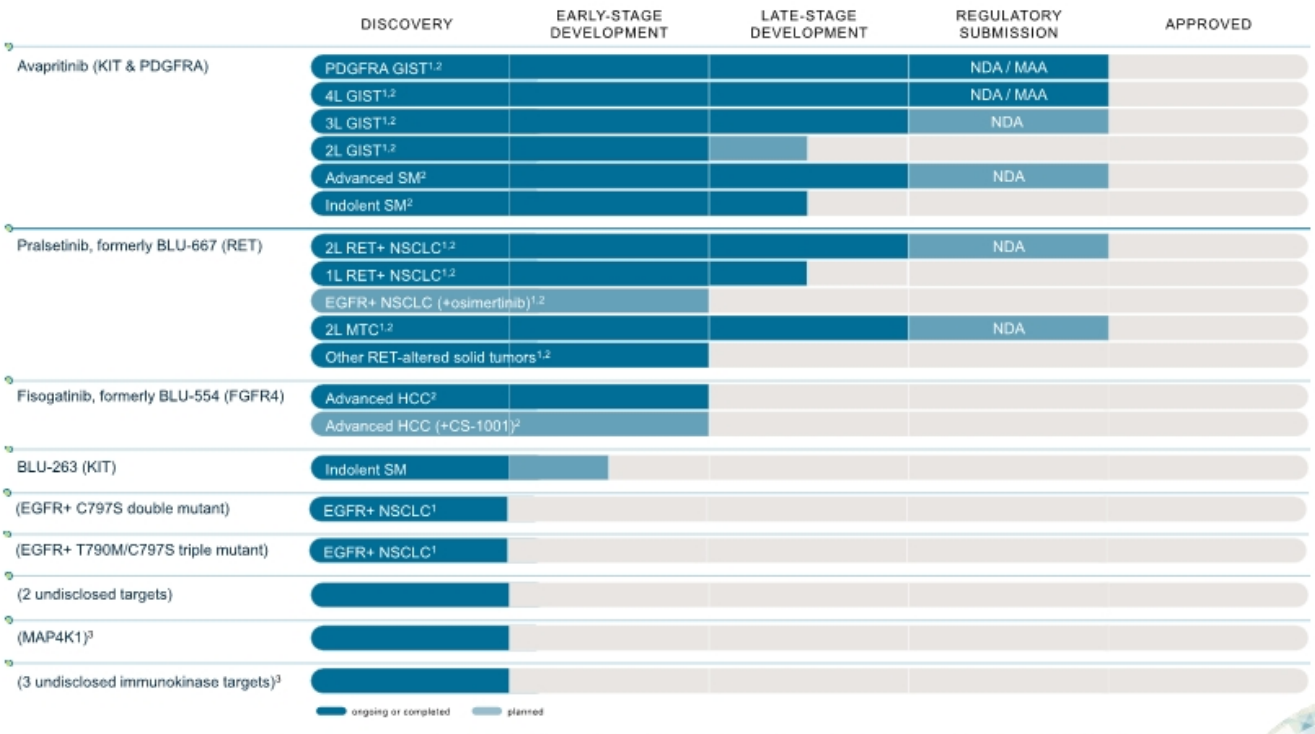
Our core mission and foundational principles

Blueprint Medicines aims to deliver
on the promise of precision medicine to improve and extend
the lives of patients with cancer and rare diseases.

HIGHLY SELECTIVE INHIBITORS

PATIENT SELECTION

ADAPTIVE ABILITY



1. Unresectable or metastatic disease. 2. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, pralsetinib and fisogatinib in Mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains all rights in the rest of the world. 3. In collaboration with Roche. Blueprint Medicines has U.S. commercial rights for up to two programs; Roche has worldwide commercialization rights for up to two programs and ex-U.S. commercialization rights for up to two programs. 1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line; GIST, gastrointestinal stromal tumors; HCC, hepatocellular carcinoma; MTC, medullary thyroid cancer; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis.

Comprehensive systemic mastocytosis clinical trial program

EXPLORER

Advanced SM

Phase 1 dose-escalation trial
with open-label expansion

PATHFINDER

Advanced SM

Phase 2 single-arm trial

PIONEER

Indolent SM

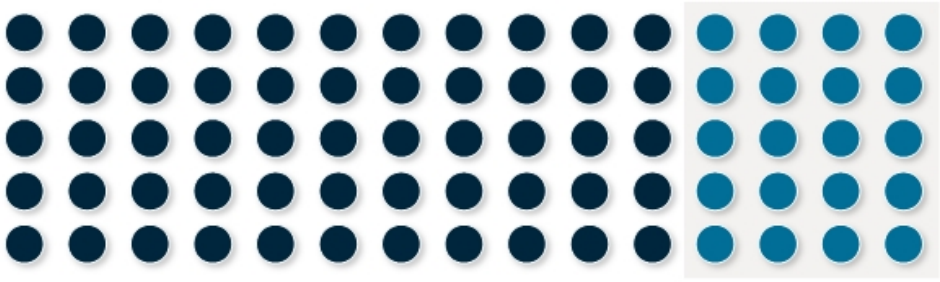
Phase 2 randomized, double-blind,
placebo-controlled trial

Systemic mastocytosis represents a significant opportunity

SYSTEMIC MASTOCYTOSIS EPIDEMIOLOGY

~75,000

prevalent patients in major markets[1]



~20,000 patients are identifiable within claims data in the United States[2]

MOST ADULTS WITH CUTANEOUS SYMPTOMS WILL SHOW SYSTEMIC DISEASE WHEN FULLY INVESTIGATED

Major markets include US, EU5 (France, Germany, Italy, Spain and the United Kingdom) and Japan. 1. Cohen S et al Br J Haematol (2014) 166(4):521-8 and World Bank Population estimates. 2. Blueprint Medicines analysis of claims data for mastocytosis.

PIONEER: A Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study of Avapritinib in Patients with Indolent or Smoldering Systemic Mastocytosis with Symptoms Inadequately Controlled with Standard Therapy

Cem Akin, Vito Sabato, Jason Gotlib, Mariana Castells, Michael W. Deininger, Hanneke Oude Elberink, Mark L. Heaney, Paul van Daele, Deepti Radia, Massimo Triggiani, Daniel J. DeAngelo, Iván Alvarez-Twose, Sigurd Broesby-Olsen, Tracy I. George, Karin Hartmann, Frank Siebenhaar, Andreas Reiter, Peter Vadas, Patrizia Bonadonna, Jens P. Panse, Petra Staubach-Renz, Knut Brockow, Diamant Thaci, Hui-Min Lin, Andrew Morrison, Brenton Mar, Marcus Maurer

American Society of Hematology Annual Meeting
Orlando, FL, USA, December 8, 2019

PIONEER
Indolent & Smoldering SM

Disclosures

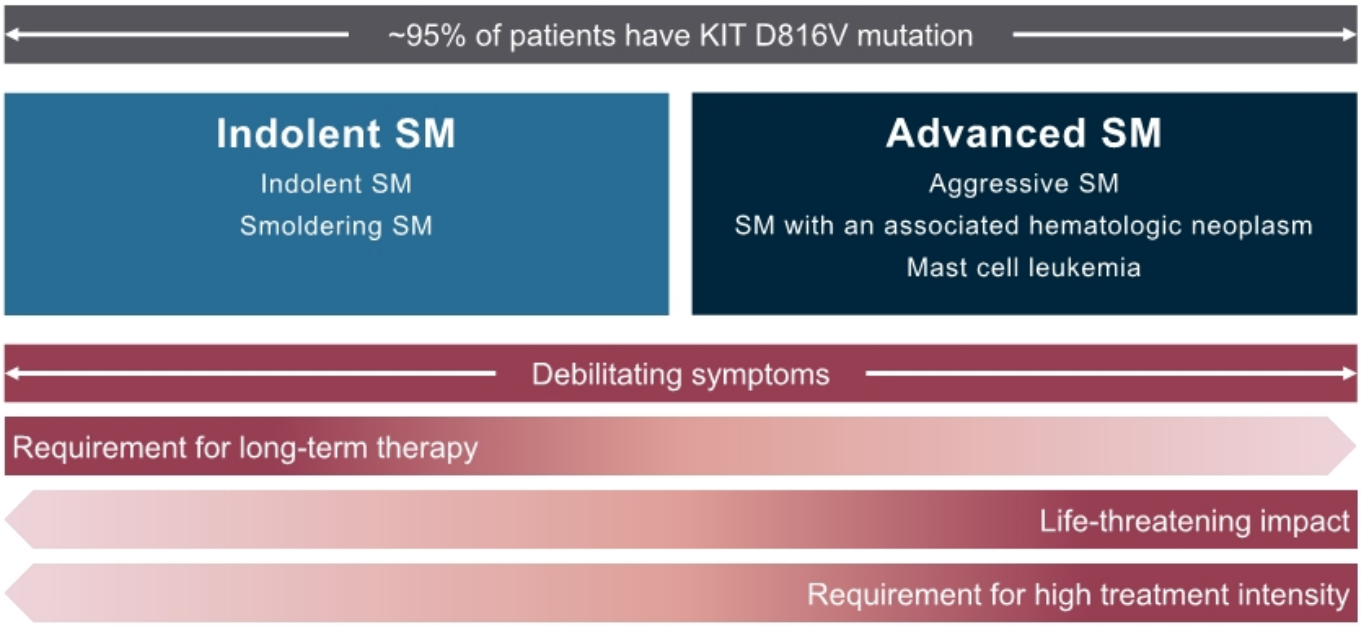
Dr. DeAngelo is an investigator on Blueprint Medicines' ongoing EXPLORER and PATHFINDER trials in advanced SM and ongoing PIONEER trial in indolent SM

Consultant: Blueprint Medicines, Celgene, Incyte, Jazz Pharmaceuticals, Novartis, Pfizer, Shire

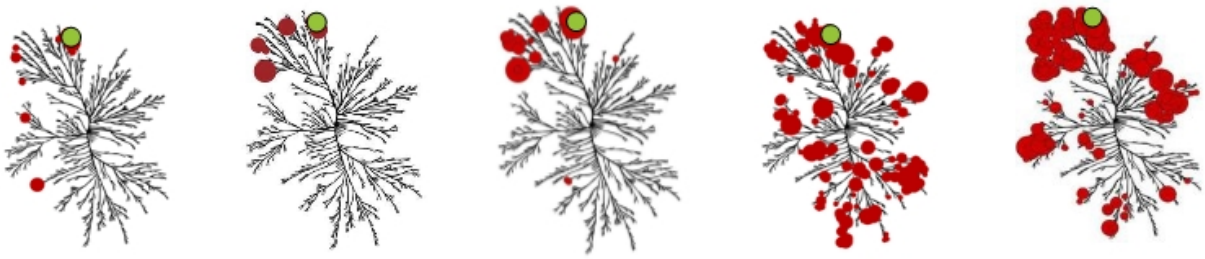
Research funding: AbbVie, Amgen, GlycoMimetics, Novartis, Takeda Pharmaceuticals

Avapritinib is an investigational agent being developed by Blueprint Medicines and has not been approved by the U.S. Food and Drug Administration or any other health authority for use in the United States or any other jurisdiction for any indication

Systemic mastocytosis is one disease with a common genetic driver



Avapritinib potently and selectively targets KIT D816V



Binding to KIT Binding to other kinases (size is proportional to binding)

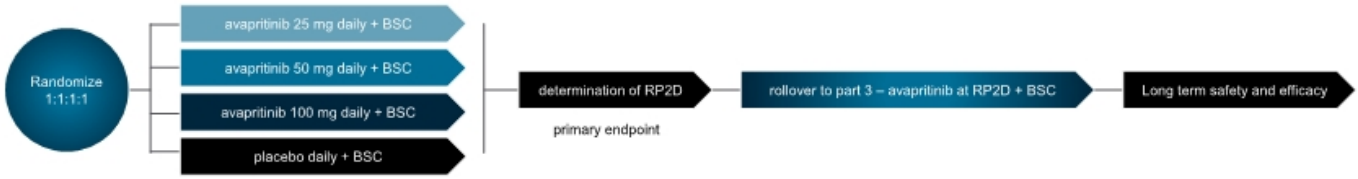
KIT D816V biochemical IC_{50}				
avapritinib*	imatinib*	masitinib#	midostaurin*	ripretinib#
0.27 nM	8150 nM	>1000 nM	2.9 nM	2.6 nM

Biochemical binding by DiscoverRX at 3uM

*Evans EK et al. Sci Transl Med. 2017;9(414). #Blueprint Medicines internal data on file. Kinome illustrations reproduced courtesy of Cell Signaling Technology, Inc. (CSTI) (www.cellsignal.com). Blueprint Medicines is not responsible for the content of the CSTI site. The trademarks appearing in this presentation are the property of their respective owners.

Phase 2 PIONEER clinical trial in patients with indolent SM

Part 1: Dose Selection (fully enrolled)



After analysis of Part 1 and determination of RP2D, Part 2 opens enrollment

Part 2: Pivotal Efficacy (pending)

Key Eligibility Criteria

- Age ≥18 years, ECOG performance status 0–2
- Indolent SM or smoldering SM confirmed by central pathology review of bone marrow biopsy, according to WHO criteria
- Moderate-to-severe symptoms based on minimum mean TSS over the 14-day eligibility screening period for assessment of TSS
- ≥1 symptom in skin or GI domains of the ISM-SAF at baseline
- Failed to achieve symptom control for ≥1 symptom as measured by the ISM-SAF with ≥2 symptomatic therapies

BSC, best supportive care; ECOG, Eastern Cooperative Oncology Group; GI, gastrointestinal; ISM-SAF, indolent systemic mastocytosis symptom assessment form; RP2D, recommended part 2 dose; TSS, total symptom score; WHO, World Health Organization.

Baseline patient demographics, disease characteristics and disposition

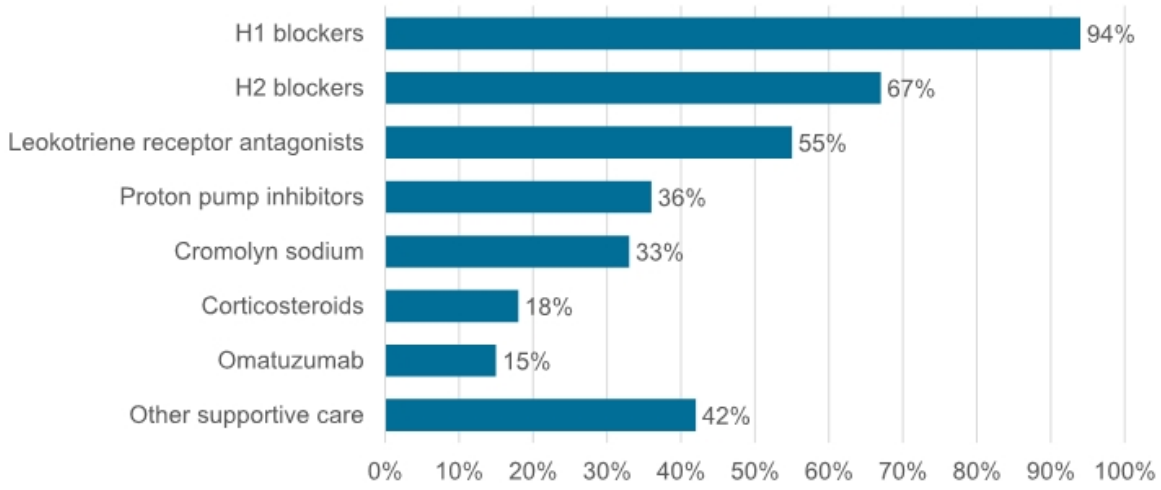
Patient demographics	All doses (N=39)
Age (years), Median (range)	51 (21–75)
Sex, n (%), Female	30 (77)
ECOG PS, n (%), 0-1	31 (79)
2	8 (21)

Disease characteristics	
Tryptase, µg/L, Mean (SD)	84 (101)
Median (range)	45 (6–416)
ISM-SAF TSS, 0-110, Median (range)	52 (19–100)
Bone marrow core biopsy MC, %	
Mean (SD)	16 (15)
Median (range)	10 (1–60)

Patient disposition, n (%)	All doses (N=39)
Weeks on study, Median (range)	12 (1–30)
Still on study	37 (95)
Discontinued study	2 (5)
Patient decision, non-compliance	1, 1

PIONEER data presented at ASH 2019 Annual Meeting. Data cutoff: November 12, 2019. MC, mast cells; PS, performance status; SD, standard deviation.

Baseline best supportive care medications recorded



Baseline BSC medications recorded for 33 patients (85%) as of data cutoff

Median number BSC medications: 3 (range: 1–7)

PIONEER data presented at ASH 2019 Annual Meeting. Data cutoff: November 12, 2019.

ISM-SAF a content-valid patient-reported outcomes tool for ISM

Design and Validation

ISM-SAF was designed with input from disease experts, patients and regulatory authorities[1]

- ✓ Concept elicitation and questionnaire construction
- ✓ Questionnaire evaluation
- ○ Validation (ongoing)
- ○ Score interpretation (ongoing)

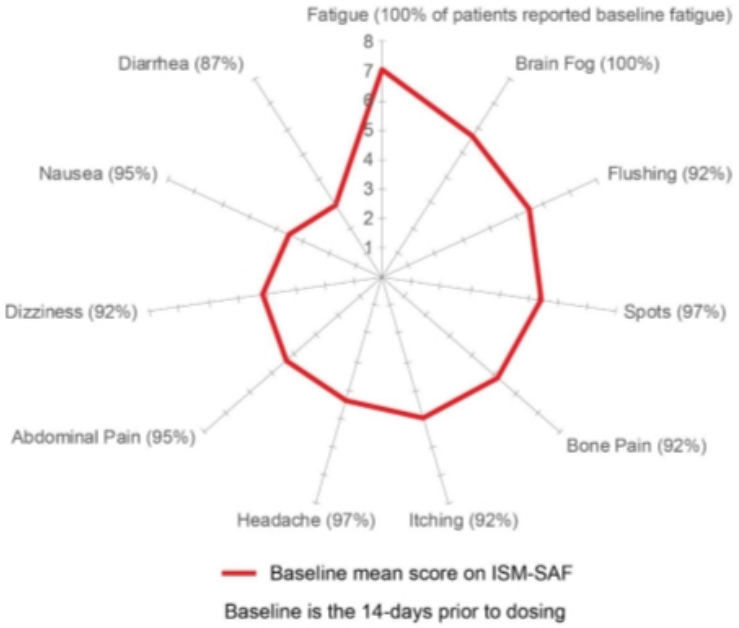
Symptom Assessment Form (SAF)

(all scores analyzed as last 14 days moving average)

Symptom	Domains	Score
Abdominal pain	GI domain	0-10 scored daily
Diarrhea		
Nausea		
Spots	Skin domain	
Itching		
Flushing		
Brain Fog		
Headache		
Dizziness		
Bone pain		
Fatigue		

Total Symptom Score (TSS) 0-110

Baseline sign and symptom burden in patients enrolled in PIONEER



- Significant symptom burden in every patient enrolled
- 84% of screened patients met minimum symptom burden eligibility requirement
- Baseline median Total Symptom Score was 52 (range: 19–100)
- Most severe symptoms in the 14 days prior to dosing were fatigue, brain fog, and flushing
- Least severe symptom, diarrhea, still occurred in 87% of patients in the 14 days prior to dosing

PIONEER data presented at ASH 2019 Annual Meeting. Data cutoff: November 12, 2019.

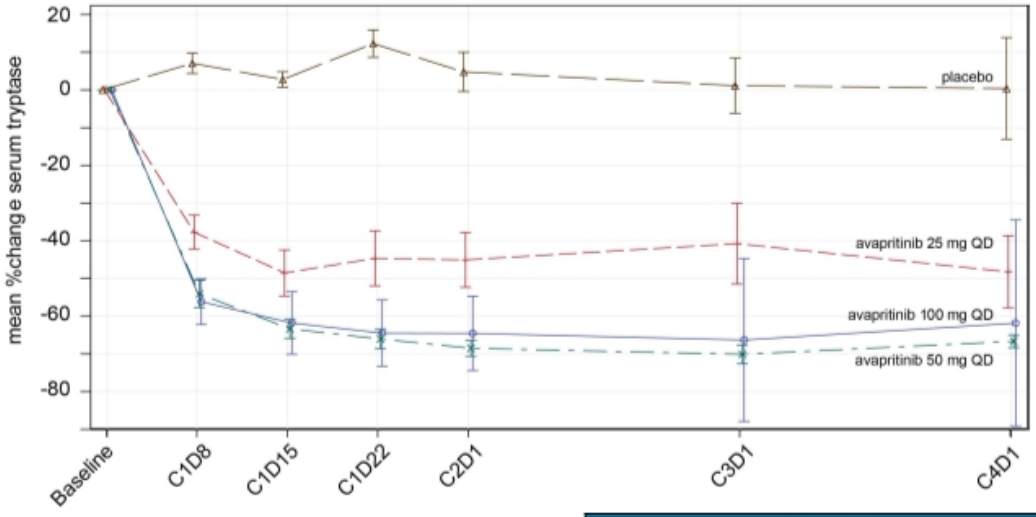
Treatment-emergent adverse events (>10%), any grade

		avapritinib			
Preferred term, n (%)	**Placebo n=9**	**25 mg n=10**	**50 mg n=10**	**100 mg n=10**	**Total n=30**
Number of subjects with ≥1 TEAE	8 (89)	9 (90)	8 (80)	8 (80)	25 (83)
Nausea	2 (22)	0	6 (60)	3 (30)	9 (30)
Headache	1 (11)	2 (20)	2 (20)	3 (30)	7 (23)
Dizziness	1 (11)	2 (20)	1 (10)	3 (30)	6 (20)
Diarrhea	1 (11)	0	3 (30)	2 (20)	5 (17)
Fatigue	1 (11)	2 (20)	1 (10)	1 (10)	4 (13)
Face edema	0	1 (10)	0	3 (30)	4 (13)

- No patients discontinued treatment due to an AE
- No intracranial bleeding, thrombocytopenia or anemia reported
- Grade 3 AEs: 2 (22.2%) patients in the placebo cohort versus 5 (16.7%) patients across all avapritinib cohorts
- Serious AEs: 2 (22.2%) patients in the placebo cohort versus 0 patients across all avapritinib cohorts
- 1 grade 3 cognitive effect in the 100mg cohort, which resolved following dose modification; the patient remains on therapy

PIONEER data presented at ASH 2019 Annual Meeting. Data cutoff: November 12, 2019. AE, adverse event. TEAE, treatment-emergent adverse event.

Percent change in serum tryptase from baseline by dose cohort



		Avapritinib		
Timepoint	**Placebo**	**25 mg**	**50 mg**	**100 mg**
Cycle 1, Day 8 (first post-baseline assessment)	7.05%	-37.72%	-54.08%	-56.16%
Cycle 4, Day 1 (end of week 12)	0.39%	-48.24%	-66.67%	-61.83%

PIONEER data presented at ASH 2019 Annual Meeting. Data cutoff: November 12, 2019. QD, once daily.

Summary of initial data from PIONEER trial Part 1

- At baseline, patients had moderate to severe symptoms despite best supportive care medications
  - The most severe patient-reported symptoms were fatigue, brain fog, flushing and cutaneous symptoms
- Treatment with avapritinib at 25, 50 and 100 mg QD resulted in rapid decreases in serum tryptase
- Avapritinib was well-tolerated in patients with indolent SM
  - No patient discontinued treatment with avapritinib due to an adverse event
  - The most common AEs (avapritinib; placebo) were nausea (30%; 22%), headache (23%; 11%) and dizziness (20%; 11%)
  - SAEs occurred in 0% of avapritinib-treated patients and 22% of placebo-treated patients
- The registration-enabling Part 2 is anticipated to begin patient screening in the first half of 2020

PIONEER data presented at ASH 2019 Annual Meeting. Data cutoff: November 12, 2019.

Systemic mastocytosis development program update

Andy Boral, MD, PhD

Chief Medical Officer

blueprint MEDICINES

Initial PIONEER data reinforce opportunity for avapritinib in indolent SM

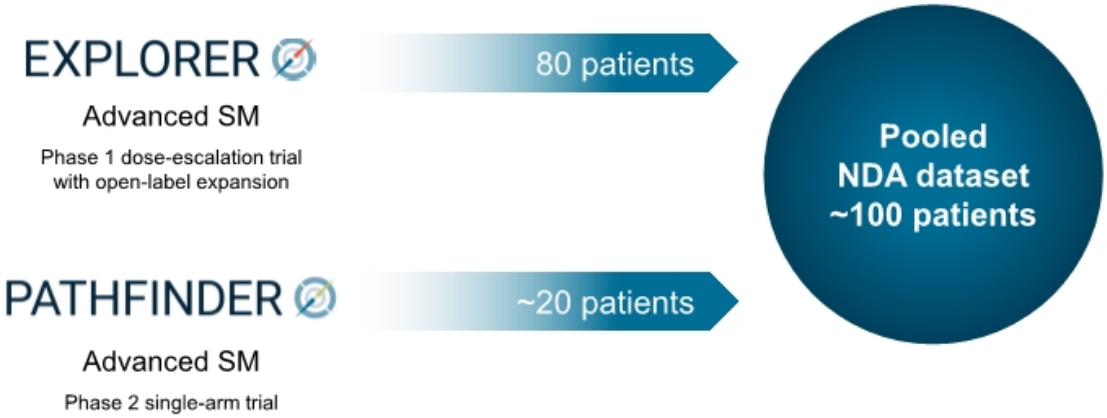
- Indolent SM population is larger than initially understood
- High symptom burden despite best available therapy
- Avapritinib is the only KIT D816V targeted therapy in clinical development
- Robust activity observed at all dose levels tested
- Safety data support development of low doses for chronic treatment
- Opportunity for fast, efficient clinical path to registration

PIONEER data presented at ASH 2019 Annual Meeting. Data cutoff: November 12, 2019.

Next steps for PIONEER trial of avapritinib in indolent SM

- ✓ Complete enrollment of dose-finding Part 1
- ✓ Report initial safety and serum tryptase data reported at ASH 2019
- ○ Plan to report additional Part 1 data, including patient-reported symptoms, and select the RP2D in Q1 2020
- ○ Plan to initiate patient screening in the registration-enabling Part 2 in 1H 2020

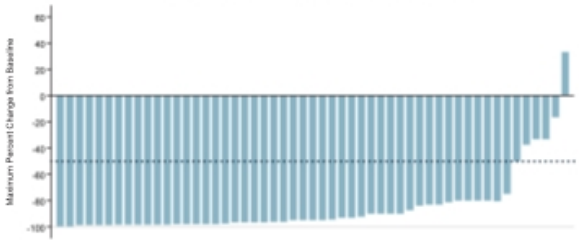
Plan to submit NDA for avapritinib for advanced SM in Q1 2020 based on combined data from EXPLORER and PATHFINDER trials



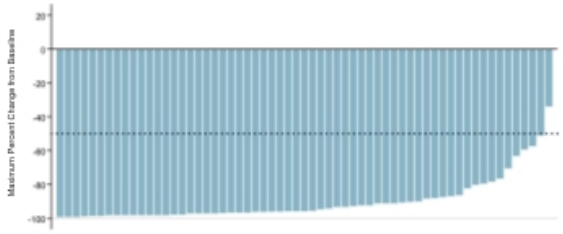
ENROLLMENT TARGETS REACHED IN BOTH EXPLORER AND PATHFINDER TRIALS

Top-line EXPLORER data: decline in mast cell burden in nearly all patients

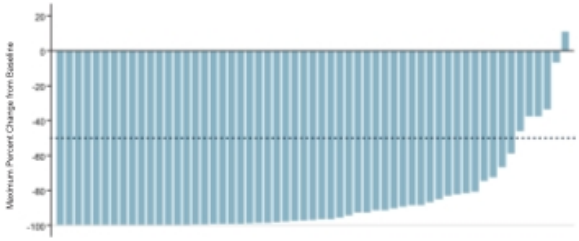
Bone marrow mast cells



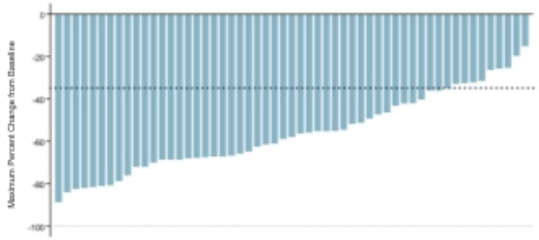
Serum tryptase



KIT D816V mutant allele fraction



Spleen volume



Top-line EXPLORER trial data reported on December 8, 2019. Data cutoff: August 30, 2019.

Top-line EXPLORER data: high rate and prolonged duration of response

BEST RESPONSE PER IWG-MRT-ECNM CRITERIA
ALL DOSES (N=48)[1]

- FDA breakthrough therapy designation[3]
- Robust activity across all disease subtypes
- Median follow up of 21 months with ongoing treatment up to ~3.5 years[1]

SAFETY
ALL DOSES (N=80)[1]

- Top-line safety results were consistent with those previously reported[4]
- Avapritinib was generally well-tolerated, and most AEs were grade 1 or 2
- The most common treatment-emergent AEs were periorbital edema, anemia, diarrhea, fatigue, peripheral edema, nausea, thrombocytopenia, vomiting and cognitive effects
- Across all doses, 6 patients discontinued treatment due to treatment-related AEs

1. Top-line EXPLORER trial data reported on December 8, 2019. Data cutoff: August 30, 2019. 2. ORR defined as complete remission with full or partial recovery of peripheral blood counts, partial remission or clinical improvement. 3. Avapritinib granted Breakthrough Therapy Designation for the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia. 4. 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. DOR, duration of response; ORR, overall response rate; OS, overall survival.

BLU-263 is a next-generation KIT inhibitor designed to enable chronic therapy in a broad population of patients with mast cell disorders

POTENT
Sub-nanomolar potency against KIT D816V

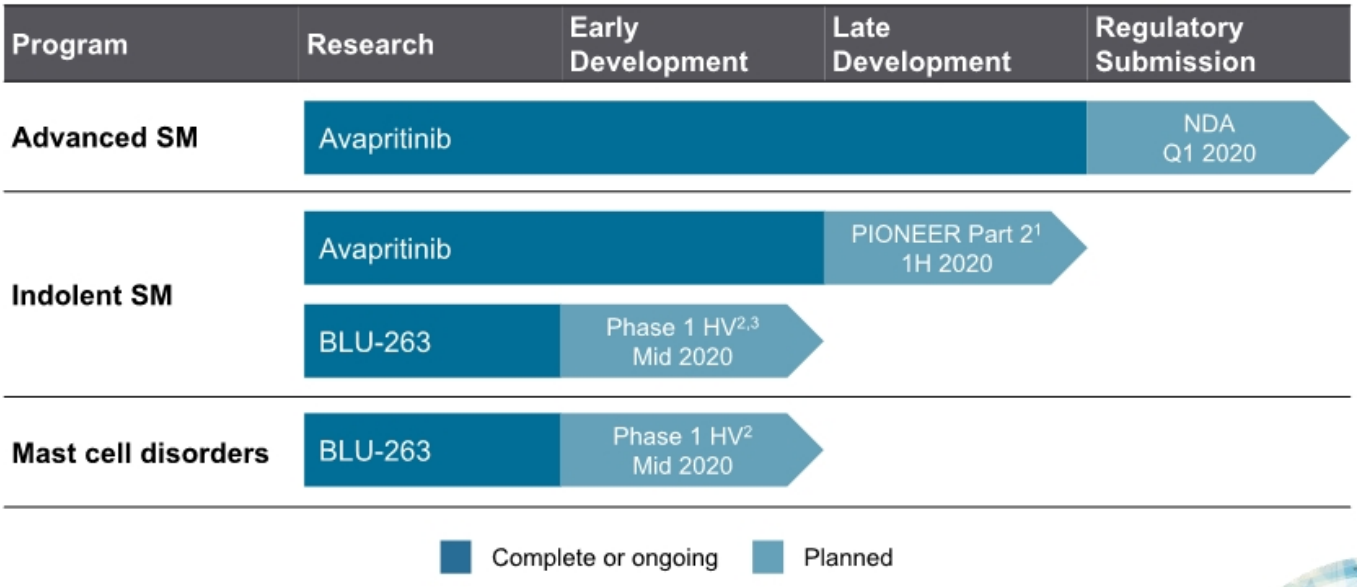
SELECTIVE
Highly selective for KIT, with low off-target activity

CNS PROFILE
Designed to not cross blood-brain barrier

PLAN TO INITIATE PHASE 1 TRIAL IN HEALTHY VOLUNTEERS IN MID 2020

CNS, central nervous system.

A comprehensive development program designed to address a broad population of patients with mast cell disorders



1. Plan to initiate patient screening in the registration-enabling Part 2 of the PIONEER trial in 1H 2020.
2. Plan to initiate Phase 1 trial of BLU-263 in healthy volunteers in mid 2020. HV, healthy volunteers.
3. Plan to submit an investigational new drug application for BLU-263 for indolent SM in 1H 2020.

Q&A

Closing remarks

Jeff Albers

Chief Executive Officer

Anticipated near-term milestones for SM, GIST and RET programs

Program	Milestone and anticipated timing
Avapritinib and BLU-263 *Systemic mastocytosis*	• Submit NDA for avapritinib for advSM in Q1 2020 • Report additional data from Part 1 of PIONEER trial in ISM in Q1 2020 • Initiate patient screening in Part 2 of PIONEER trial in ISM in 1H 2020 • Initiate Phase 1 trial of BLU-263 in healthy volunteers in mid 2020
Avapritinib *Gastrointestinal stromal tumors*	• February 14, 2020 PDUFA date for PDGFRA GIST NDA • Report top-line VOYAGER trial data in 3L GIST in Q2 2020 • Expect PDUFA date for 4L+ GIST NDA in Q2 2020
Pralsetinib *RET-altered cancers*	• Initiate Phase 3 trial in 1L NSCLC by the end of 2019 • Submit NDA for previously treated NSCLC in Q1 2020 • Submit NDA for previously treated MTC in 1H 2020

AdvSM, advanced systemic mastocytosis. ISM, indolent SM.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