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 4, 2016**

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.)

38 Sidney Street, Suite 200 **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))

Item 8.01 Other Events.

On December 4, 2016, Blueprint Medicines Corporation (the "Company") issued a press release announcing initial data from the dose escalation stage of its ongoing Phase 1 clinical trial evaluating BLU-285 for the treatment of advanced systemic mastocytosis ("SM"). BLU-285 is an orally available, potent and highly selective inhibitor that targets D816V mutant KIT. The Company presented the data on December 4, 2016 in an oral presentation at the 2016 American Society of Hematology ("ASH") Annual Meeting and Exposition in San Diego, California. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and incorporated herein by reference. A copy of the presentation is attached as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein by reference.

Cautionary Note Regarding Forward-Looking Statements

This Current Report on Form 8-K 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 clinical development of BLU-285; the Company's ability to implement its clinical development plans for BLU-285 for the treatment of advanced SM; and the Company's ability to enroll patients in its ongoing Phase 1 clinical trial for BLU-285 in advanced SM. 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 Current Report on Form 8-K 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 Current Report on Form 8-K, including, without limitation, risks and uncertainties related to the delay of any current or planned clinical trials or the development of BLU-285; the Company's advancement of multiple early-stage efforts; the Company's ability to successfully demonstrate the efficacy and safety of its drug product candidates; the preclinical and clinical results for the Company's drug product candidates, which may not support further development of such drug product candidates; and actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; the Company's ability to develop and commercialize companion diagnostics for its current and future drug candidates; and the success of the Company's rare genetic disease collaboration with Alexion Pharma Holding and its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, as filed with the Securities and Exchange Commission ("SEC") on November 10, 2016, and other filings that Blueprint Medicines may make with the SEC in the future. Any forward-looking statements contained in this Current Report on Form 8-K represent the Company's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. The Company explicitly disclaims any obligation to update any forward-looking statements.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press release issued by Blueprint Medicines Corporation on December 4, 2016
99.2	Presentation by Blueprint Medicines Corporation on December 4, 2016 at the ASH Annual Meeting and Exposition

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 5, 2016

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

EXHIBIT INDEX

Exhibit No.	Description
99.1	Press release issued by Blueprint Medicines Corporation on December 4, 2016
99.2	Presentation by Blueprint Medicines Corporation on December 4, 2016 at the ASH Annual Meeting and Exposition

Blueprint Medicines Announces Proof-of-Concept Data from Phase 1 Clinical Trial of BLU-285 in Patients with Advanced Systemic Mastocytosis

– Favorable Safety and Tolerability Profile –
– Decreased Bone Marrow Mast Cell Burden in 6 of 8 Evaluable Patients –
– Decreased Serum Tryptase in 10 of 12 Patients –
– Blueprint Medicines to Host Investor Conference Call and Webcast on Monday, December 5, at 8:00 a.m. ET –

CAMBRIDGE, Mass., December 4, 2016 – Blueprint Medicines Corporation (NASDAQ: BPMC), a leader in discovering and developing targeted kinase medicines for patients with genomically defined diseases, today announced data from its ongoing Phase 1 trial evaluating BLU-285, an investigational medicine for the treatment of patients with advanced systemic mastocytosis (SM). Blueprint Medicines is developing BLU-285 as a potent, highly selective inhibitor of D816V mutant KIT. Approximately 90 to 95 percent of patients with SM are estimated to have the KIT D816V mutation, the key driver of SM that triggers the abnormal proliferation and survival of mast cells. The data are being presented today at the 2016 American Society of Hematology (ASH) Annual Meeting and Exposition in San Diego, California.

“Advanced systemic mastocytosis is a rare and severe disease that shortens life expectancy with a wide range of debilitating symptoms and organ damage,” said Daniel DeAngelo, M.D., Dana-Farber Cancer Institute, an investigator on the clinical trial. “We need new treatment options that address the underlying cause of the disease and can improve the significant symptoms that impact patients’ daily lives. The objective decreases in mast cell burden and improvements in symptoms seen in the early data for this Phase 1 study are encouraging. We believe that BLU-285 has the potential to change the treatment paradigm for patients affected by advanced systemic mastocytosis.”

“We are excited by these early data demonstrating a favorable safety profile as well as signs of clinical activity starting at the first dose level,” said Andy Boral, M.D., Chief Medical Officer at Blueprint Medicines. “The decreases in bone marrow mast cell burden and serum tryptase, which are indications of clinical activity, along with the fact that ten of 12 patients remain on the study, are encouraging and support the hypothesis that D816V mutant KIT is a driver of this disease. We look forward to the continued evaluation of our investigational medicine BLU-285, which we believe has the potential to be transformative for patients with advanced SM.”

Data from the Ongoing Phase 1 Clinical Trial

BLU-285 is currently being evaluated in the dose escalation portion of a Phase 1 clinical trial in patients with advanced SM. As of the data cutoff date of November 11, 2016, 12 patients had been treated at three dose levels (30 mg, 60 mg and 100 mg once daily (QD)). The median age was 61.5 years (ranging from 39 to 82), and the KIT D816V mutation has been confirmed in bone marrow or blood from 11 of the 12 patients. Ten of the 12 patients remained on the clinical trial as of the data cutoff date.

Consistent with preliminary data reported by Blueprint Medicines from its Phase 1 clinical trial for patients with advanced gastrointestinal stromal tumors (GIST), BLU-285 demonstrated a favorable pharmacokinetic profile with a half-life that supports QD dosing.

Preliminary Safety Data

As of the data cutoff date of November 11, 2016, BLU-285 was observed to be well-tolerated at all doses. No patients discontinued treatment as a result of an adverse event (AE), and no Grade 4 or worse treatment-related AEs were reported. The majority of AEs reported by investigators were Grade 1 or 2, and AEs that occurred in two or more patients were fatigue (4 patients), anemia (3 patients) and alkaline phosphatase elevation (3 patients). All three cases of alkaline phosphatase elevation were Grade 3 but were asymptomatic and transient and occurred in the absence of transaminase or bilirubin elevations. The Grade 3 alkaline phosphatase elevations occurred in the three patients with the highest bone marrow mast cell burden at baseline, suggesting this may be consistent with a pharmacodynamic effect of BLU-285 on mast cells in the bone. One of the three cases of alkaline phosphatase elevation was considered possibly treatment-related and defined as a dose-limiting toxicity at the 60 mg dose level. All three patients continued treatment with BLU-285 without a dose reduction. A maximum tolerated dose (MTD) has not been established, and enrollment in the dose escalation portion of the Phase 1 clinical trial is ongoing.

Preliminary Clinical Activity Data

As of the data cutoff date of November 11, 2016, all 12 patients treated in the first three dose levels of the dose escalation portion of the clinical trial were evaluated for signs of clinical activity.

- Investigators observed decreases in bone marrow mast cell infiltrate (measured by bone marrow biopsy) in six of the eight patients who had a bone marrow biopsy after starting treatment with BLU-285. Three of the six patients had a decrease of bone marrow mast cell infiltrate of more than 50% from baseline, including one patient with no residual mast cells in the bone marrow.

- Based on measurements at a central laboratory, serum tryptase decreased in ten of 12 patients. The serum tryptase decrease was greater than 50% in eight patients.

- The allele burden of D816V mutant KIT decreased within the first two treatment cycles in five of six patients in circulating tumor DNA and bone marrow.

- Rash improved in five patients with urticaria pigmentosa from baseline based on investigator assessments. Urticaria pigmentosa is an allergy-mediated rash common in SM patients.

- Weight increased in ten patients and albumin increased in 11 patients, suggesting improvements in malabsorption.

- Ten of 12 patients remained on treatment with treatment duration ranging from 1 month to 8.1 months.

Clinical Development Plans for BLU-285 in SM

Based on the favorable safety profile and encouraging clinical activity observed to date in the Phase 1 clinical trial for BLU-285 for the treatment of advanced SM, Blueprint Medicines plans to continue to enroll patients in the dose escalation portion of this clinical trial until an MTD is reached or a recommended dose is established. Once a recommended dose for further clinical evaluation has been determined or an MTD is reached, Blueprint Medicines plans to open enrollment in expansion cohorts for this Phase 1 clinical trial for specific subtypes of advanced SM. In addition, Blueprint Medicines plans to evaluate options to expand the clinical development of BLU-285 in other KIT-driven diseases, including possible opportunities for the treatment of indolent SM and KIT-mutant acute myeloid leukemia, groups of patients in need of more effective treatments. Blueprint Medicines is also collaborating with a health research outcomes group to develop a disease-specific patient reported outcome tool to measure changes in total symptom burden in advanced SM and indolent SM.

Conference Call Information

Blueprint Medicines will host a conference call and webcast to review the data presented at the ASH Annual Meeting and Exposition on Monday, December 5, 2016 beginning at 8:00 a.m. ET. To participate in the conference call, please dial 855-728-4793 (domestic) or 503-343-6666 (international) and refer to conference ID 10777452. An audio webcast of the call will also be available in the Investors section of Blueprint Medicines' website at http://ir.blueprintmedicines.com. The archived website will be available on Blueprint Medicines' website approximately two hours after the conference call and will be available for 30 days following the call.

About the Phase 1 Clinical Trial for BLU-285 in Advanced SM

Blueprint Medicines' Phase 1 clinical trial of BLU-285 for the treatment of advanced SM is designed to evaluate the safety and tolerability of BLU-285 in multiple ascending doses in patients with advanced SM, including aggressive SM (ASM), advanced SM with an associated hematologic neoplasm (SM-AHN) and mast cell leukemia (MCL) with the goal of establishing an MTD or a lower recommended dose if appropriate. Bone marrow and or blood samples from all patients are tested for the D816V mutation in KIT. Once the MTD is reached, or a recommended dose is established, Blueprint Medicines plans to open expansion cohorts for specific subtypes of advanced SM. Secondary objectives for this Phase 1 clinical trial include assessment of the pharmacokinetic profile of BLU-285, assessment of response rate by the International Working Group Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) criteria, changes in KIT D816V mutant allele fractions in bone marrow and circulating tumor DNA and changes in patient reported outcomes. The Phase 1 clinical trial is designed to enroll approximately 60 patients, including approximately 25 patients during dose escalation and approximately 35 additional patients in expansion cohorts, at multiple sites in the United States and the European Union. Please refer to www.clinicaltrials.gov for additional details related to this Phase 1 clinical trial. For more information, contact the study director for this Phase 1 clinical trial at studydirector@blueprintmedicines.com.

About SM

There are several forms of SM, including indolent SM and more advanced forms of SM, which include aggressive SM, SM-AHN and MCL. SM is characterized by the buildup of mast cells, which are immune cells that produce histamine and other mediators of the body's inflammatory and allergic responses. In patients with SM, mast cells release high levels of these mediators, causing symptoms that range from

mild to life-threatening symptoms, including pain, nausea, rash, fever, fatigue and anaphylaxis. In patients with advanced SM, including aggressive SM, SM-AHN and MCL, mast cell infiltration in bone marrow, liver and other vital organs can eventually lead to organ dysfunction and lower life expectancy, with a median overall survival of approximately four years or less. Patients with indolent SM do not have a lower life expectancy, but they do suffer from a broad range of acute and chronic symptoms that can have a significant impact on their quality of life. There are no approved treatments that target the KIT D816V mutation, which is the primary driver of disease in approximately 90 to 95 percent of SM patients, and there is a clear need for more effective therapies for patients with advanced SM and for patients with indolent SM who have a heavy symptom burden.

About BLU-285

BLU-285 is an orally available, potent and highly selective inhibitor of D816V mutant KIT. Blueprint Medicines is initially developing BLU-285, an investigational medicine, for the treatment of patients with advanced SM and advanced GIST. BLU-285 was discovered by Blueprint Medicines' research team leveraging its proprietary compound library, and Blueprint Medicines retains worldwide development and commercialization rights for BLU-285.

About Blueprint Medicines

Blueprint Medicines is developing a new generation of targeted and potent kinase medicines to improve the lives of patients with genomically defined diseases. Its approach is rooted in a deep understanding of the genetic blueprint of cancer and other diseases driven by the abnormal activation of kinases. Blueprint Medicines is advancing three programs in clinical development for subsets of patients with gastrointestinal stromal tumors, hepatocellular carcinoma and systemic mastocytosis, as well as multiple programs in research and preclinical development.

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 clinical development of BLU-285; Blueprint Medicines' ability to implement its clinical development plans for BLU-285 for the treatment of advanced SM; Blueprint Medicines' ability to enroll patients in its ongoing Phase 1 clinical trial for BLU-285 in advanced SM; and Blueprint Medicines' strategy, 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 product candidates, including BLU-285 and BLU-554; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' ability to successfully demonstrate the efficacy and safety of its drug product candidates; the preclinical and clinical results for Blueprint Medicines' drug product candidates, which may not support further development of such drug product candidates; and actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; Blueprint Medicines' ability to develop and commercialize companion

diagnostics for its current and future drug candidates, including companion diagnostics for BLU-554 with Ventana Medical Systems, Inc. and for BLU-285 with QIAGEN Manchester Limited; and the success of Blueprint Medicines' rare genetic disease collaboration with Alexion Pharma Holding and its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Blueprint Medicines' Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, as filed with the Securities and Exchange Commission (SEC) on November 10, 2016, and other filings that Blueprint Medicines 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. Blueprint Medicines explicitly disclaims any obligation to update any forward-looking statements.

Contact

Investor Relations:

Kristin Williams
Blueprint Medicines Corporation
617-714-6674
kwilliams@blueprintmedicines.com

Media Relations:

Rachel Hutman
W2O Group
301-801-5540
rhutman@w2ogroup.com

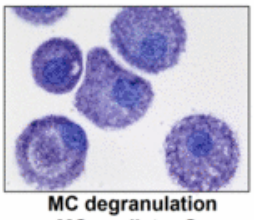

Preliminary Safety and Activity in a Phase 1 study of BLU-285, a Potent, Highly-Selective Inhibitor of KIT D816V in Advanced Systemic Mastocytosis (SM)
Mark Drummond[1], Daniel DeAngelo[2], Michael Deininger[3], Deepti Radia[4], Albert Quiery[5], Elizabeth Hexner[6], Hongliang Shi[7], Terri Alvarez-Diez[7], Erica Evans[7], Mary Ellen Healy[7], Beni Wolf[7], Srdan Verstovsek[8]
[1]Beatson West of Scotland Cancer Centre, NHS Greater Glasgow and Clyde, Glasgow, United Kingdom; [2]Dana-Farber Cancer Institute, Boston, MA; [3]Division of Hematology and Hematologic Malignancies, Huntsman Cancer Institute, The University of Utah, Salt Lake City, UT; [4]Guy's & St Thomas NHS Trust, London, United Kingdom; [5]University of Michigan, Ann Arbor, MI; [6]Abramson Cancer Center of the University of Pennsylvania, Philadelphia, PA; [7]Blueprint Medicines, Cambridge, MA; [8]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX
American Society of Hematology Annual Meeting
San Diego, California, USA,
04 Dec 2016

Advanced Systemic Mastocytosis

- **Mast cell neoplasm with poor prognosis and no effective treatments**
  - **Aggressive Systemic Mastocytosis (ASM); SM with associated hematologic neoplasm (SM-AHN); mast cell leukemia (MCL)**
- **KIT mutation D816V is a key driver in ~90-95% of patients[1]**

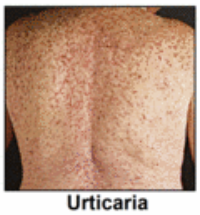
Mast cell accumulation and organ infiltration

Blood*



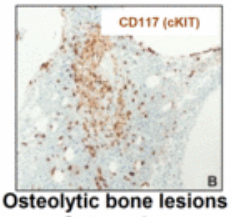
MC degranulation
MC mediator Sx
↑tryptase

Skin$



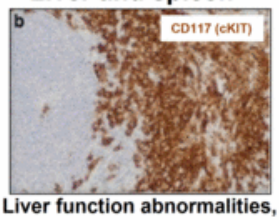
Urticaria pigmentosa

Bone and bone marrow*



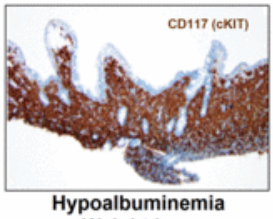
Osteolytic bone lesions
Cytopenias

Liver and spleen†



Liver function abnormalities,
Ascites, or Hypersplenism

GI tract‡



Hypoalbuminemia
Weight loss

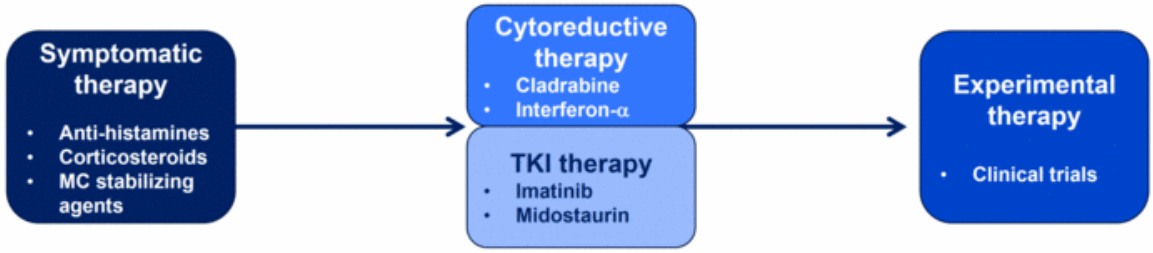
C-findings

MC, mast cell; MCL, mast cell leukemia; SM, systemic mastocytosis; C- findings, clinical findings
[1]Garcia-Montero AC et al (2006)
Images reproduced with permission from: *Metcalfe D (2016); $Hartmann K et al (2015); †Ammanagari N et al (2013); ‡Behdad A., Owens SR (2013)

Study sponsored by Blueprint Medicines Corporation

Advanced SM has High Medical Need

Current therapy does not eradicate KIT D816V



Advanced SM subtype	Life expectancy (months)
ASM	~41
SM-AHN	~24
MCL	~2

[1]Lim KH et al (2009)

- ↓Life expectancy with current therapy[1]
- Morbidity via C-findings
  - Cytopenias
  - Osteolytic bone lesions
  - Hepatomegaly with liver dysfunction
  - Hypersplenism
  - Malabsorption with weight loss

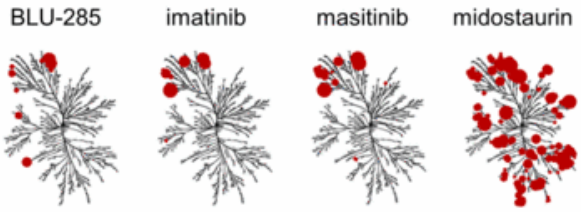
KIT, receptor tyrosine kinase protein; TKI, tyrosine-kinase inhibitor

Study sponsored by Blueprint Medicines Corporation

BLU-285: Potent, Highly Selective KIT D816V Inhibition

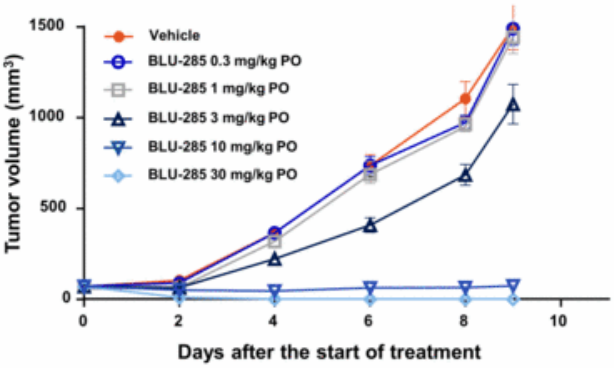
Biochemical profiles

	KIT D816V	
	IC_{50} (nM)	K_D (nM)
BLU-285	0.27	0.6
imatinib	8,150	> 10K
masitinib	> 10K	> 10K
midostaurin	2.8	3.4



IC_{50}, half maximal inhibitory concentration; K_D, dissociation constant; PO, orally
[1]Evans E et al (2014)
Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com)

Anti-tumor activity in KIT-driven mastocytoma model[1]



Model driven by KIT mutation equivalent to human KIT D816 mutation

Study sponsored by Blueprint Medicines Corporation

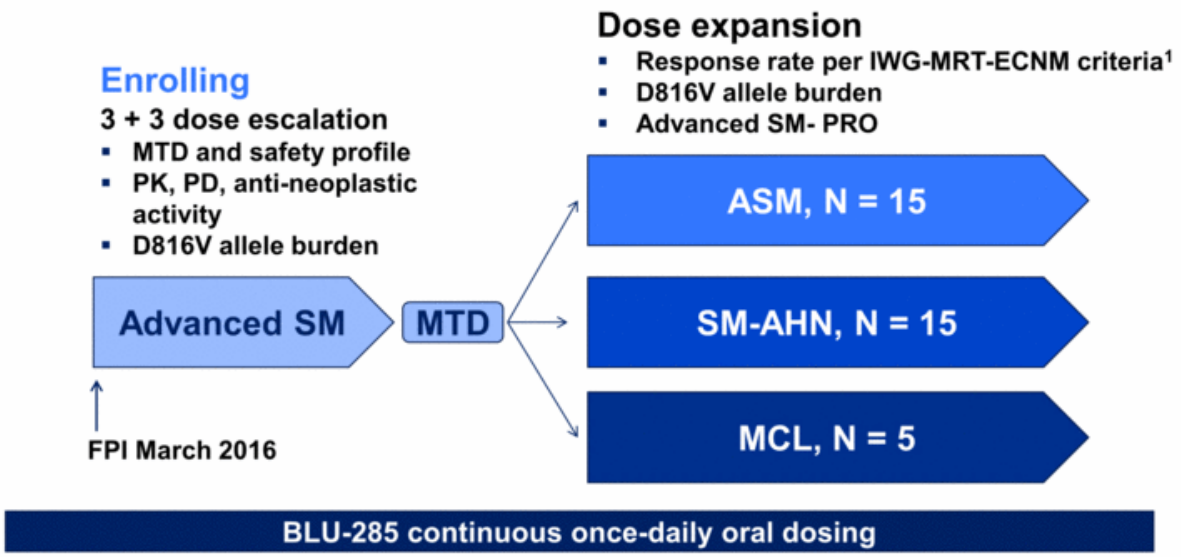
Key Entry Criteria

- Any of the following diagnoses:
  - Aggressive Systemic Mastocytosis (ASM)[1]
  - SM with associated hematologic disorder (SM-AHN)[1] with ≥ 1 C-finding
  - Mast Cell Leukemia (MCL)[1]
  - Relapsed or refractory myeloid malignancy (dose escalation only)[2]
- Age ≥ 18
- ECOG performance status 0–3
- Platelet count ≥ 25 x 10^9 /L
- ANC ≥ 0.5 x 10^9 /L
- Adequate hepatic and renal function

ANC, absolute neutrophil count; ECOG, Eastern Cooperative Oncology Group
[1]ASM, SM-AHNMD, or MCL per WHO criteria via local diagnosis and retrospective central pathology to confirm mastocytosis subtype. [2]Per IWG-MRT or WHO diagnostic criteria

Study sponsored by Blueprint Medicines Corporation

BLU-285 Phase 1 Objectives and Design



FPI, first patient-in; IWG-MRT-ECNM, International working group – myeloproliferative neoplasms research and treatment – European; competence network on mastocytosis; MTD, maximum tolerated dose; PD, pharmacodynamics; PK, pharmacokinetics; SM-PRO, systemic mastocytosis patient reported outcomes

[1]Gotlib J et al (2013); NCT02561988

Study sponsored by Blueprint Medicines Corporation

Demography and Baseline Patient Characteristics

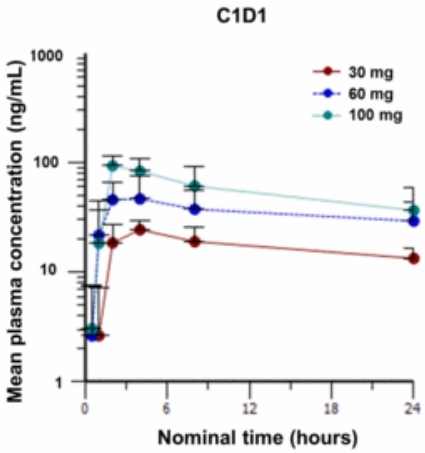
Parameter (all data are preliminary as of 11 November 2016 cutoff)	All patients, N = 12
Disease subtype per local assessment, n (%)	
ASM	8 (67)
MCL	1 (8)
SM-AHN (all AHN are CMML)	3 (25)
KIT D816V mutation, n (%)	11 (92)[1]
ECOG performance status, n (%)	
0	2 (17)
1	10 (83)
Prior anti-neoplastic therapy, n (%)	6 (50)[2]
Number of C-findings median (range)	1 (1–3)
Cytopenias, n (%)	6 (50)
Osteolytic bone lesions	2 (17)
Hepatomegaly with liver dysfunction	2 (17)
Hypersplenism	5 (42)
Malabsorption with weight loss	4 (33)
Uriticaria Pigmentosa / Other SM-related skin rash, n (%)	8 (67)

SM-CMML, systemic mastocytosis with chronic myelomonocytic leukemia; pt, patient
[1]One pt had no detectable KIT D816V mutation in blood or bone marrow; [2]2 pts had midostaurin; 1pt had cladribine; 1 pt had Pegasys; 1 pt had interferon alpha-2; 1 pt had hydroxyurea and 5-azacitidine

Study sponsored by Blueprint Medicines Corporation

Initial Dose Escalation and PK Results

BLU-285 mg/day	Patients treated N = 12	DLT
30	3	0
60	6	1
100	3	0
130	Enrolling	



- Dose-dependent increase in exposure
- Rapid absorption: t_{max} 2–4 hours
- Half-life > 19 hours supports QD dosing

C1D1, cycle 1 day 1; DLT, dose limiting toxicity; t_{max}, time at which C_{max} is observed; QD, once daily

Study sponsored by Blueprint Medicines Corporation

Adverse Events

Non-hematological adverse events ≥ 2 patients (safety population, N = 12)		
Adverse event	Any grade n (%)	Grade 3 n (%)
Fatigue	4 (33)	0
↑ Alkaline Phosphatase	3 (25)	3 (25)
Diarrhea	2 (17)	0
Dizziness	2 (17)	0
Headache	2 (17)	0
Nausea	2 (17)	0
Pruritus	2 (17)	0

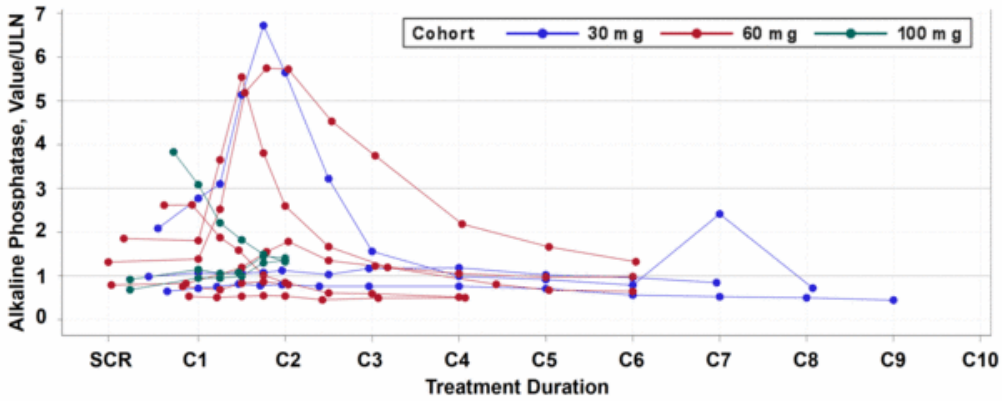
Hematological adverse events (safety population, N = 12)		
Adverse event	Any grade n (%)	Grade 3 n (%)
Anemia	3 (25)	0
Thrombocytopenia	2 (17)	1 (8)
Neutropenia	0	0

- Most AEs were CTCAE Grade 1 or 2
- No Grade 4 or 5 treatment-related events and no dose reductions required for toxicity
- 1 DLT : Grade 3 alkaline phosphatase elevation
- MTD has not been reached

AE, adverse event; CTCAE, common terminology criteria for adverse events; MTD, maximum tolerated dose

Study sponsored by Blueprint Medicines Corporation

Alkaline Phosphatase Elevation is Likely a PD Effect on Bone Marrow Mast Cells

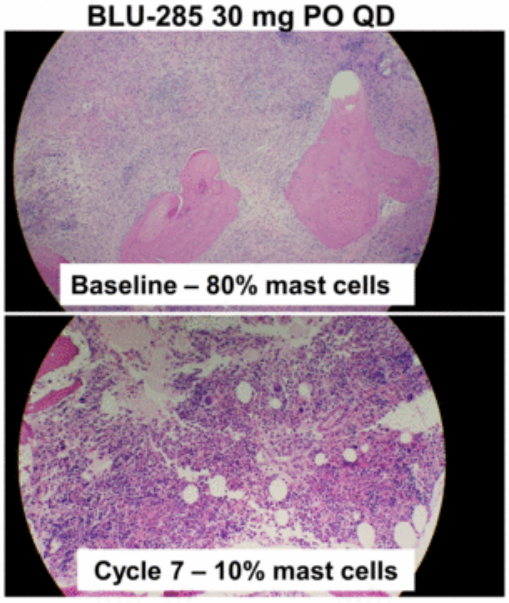


- Asymptomatic, transient Grade 3 alkaline phosphatase elevation occurred in the 3 patients with highest baseline bone marrow (BM) MC burden
- No associated transaminase or bilirubin elevation
- Confirmed bone origin in 1 patient (2 others not assessed)
- May represent a PD effect on BM MCs
- Protocol amended to consider only Grade 4 alkaline phosphatase elevation a DLT

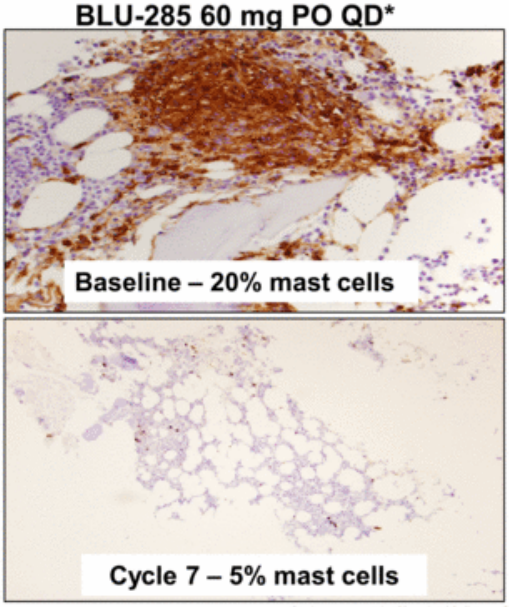
Study sponsored by Blueprint Medicines Corporation

BLU-285 Markedly Reduces Bone Marrow Mast Cells

Aggressive Systemic Mastocytosis
BLU-285 30 mg PO QD



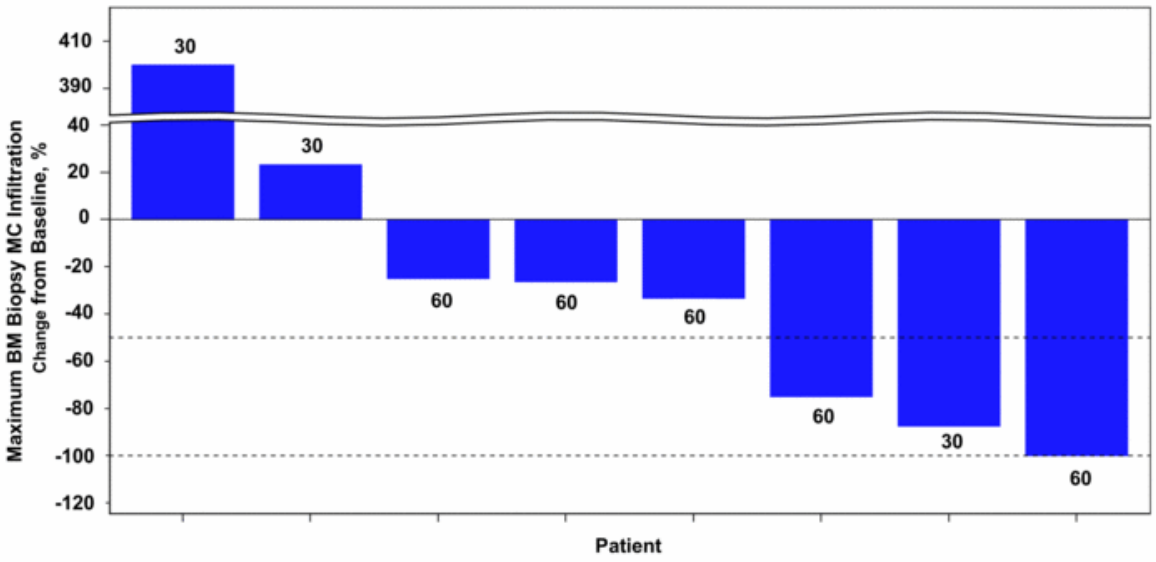
Aggressive Systemic Mastocytosis
BLU-285 60 mg PO QD*



*Dr. Mohamed E. Salama, Hematopathology Huntsman Cancer Institute University of Utah

Study sponsored by Blueprint Medicines Corporation

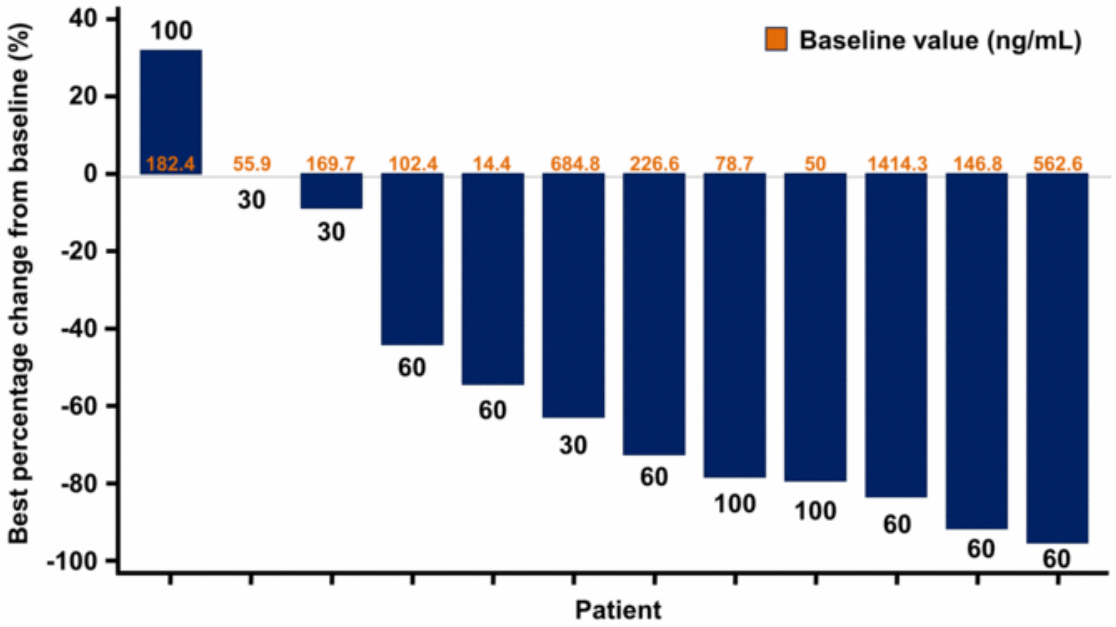
Decreased BM MCs in 6 of 8 Patients



BM, bone marrow
NB: The values above/below the bars denote the dose level (mg) QD received by each patient

Study sponsored by Blueprint Medicines Corporation

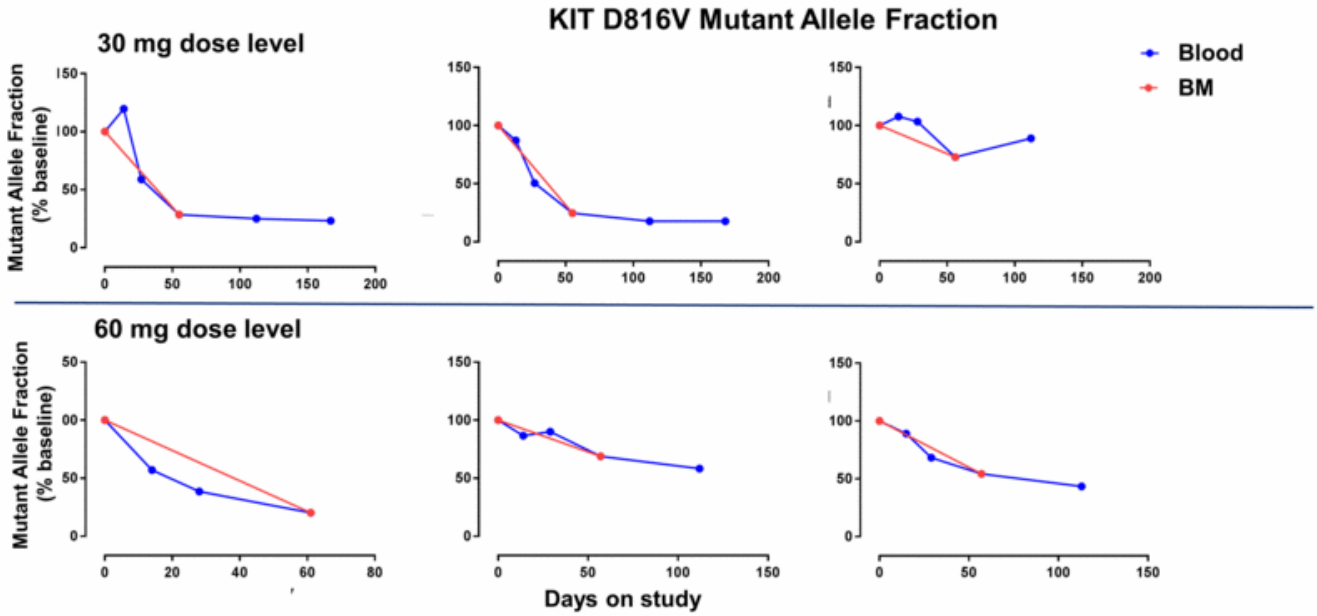
Decreased Tryptase in 10 of 12 Patients



NB: The values above/below the bars denote the dose level (mg) QD received by each patient

Study sponsored by Blueprint Medicines Corporation

Molecular Response in Blood and BM



All available data as of data cutoff date shown

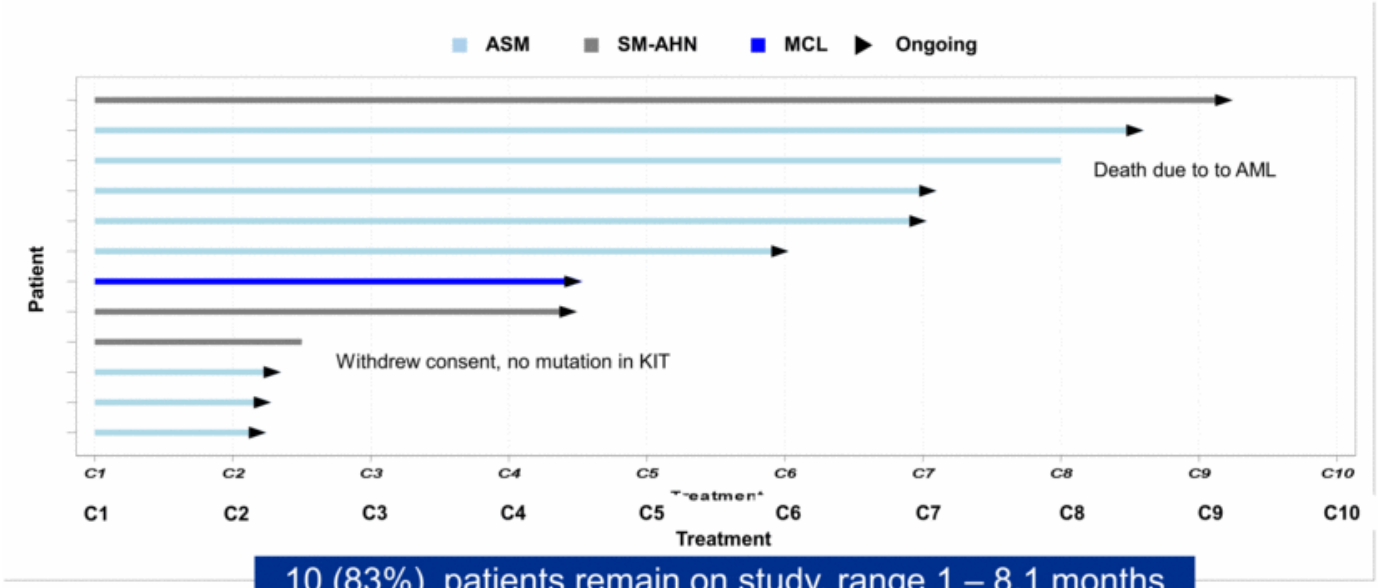
Study sponsored by Blueprint Medicines Corporation

Decreased Malabsorption and Rash

- Maximum weight gain from baseline (n =12):
  - Increase median 4.3 kg, range -0.5 – 12.9 kg
  - % increase median 4.7%, range -0.5 – 19.2%
- Maximum albumin gain from baseline (n = 12):
  - Increase median 0.45 g/dL, range 0 – 1.4 g/dL
  - % increase median 10.7%, range 0 – 40.0%
- Rash improved per investigator assessment in all 5 patients with Uriticaria Pigmentosa for whom data are available

Study sponsored by Blueprint Medicines Corporation

BLU-285 Duration on Study



10 (83%) patients remain on study, range 1 – 8.1 months

ASM, aggressive systemic mastocytosis; MCL, mast-cell leukemia; SM-AHN, systemic mastocytosis with an associated hematologic neoplasm

Study sponsored by Blueprint Medicines Corporation

Summary

- BLU-285 has demonstrated encouraging clinical activity in advanced SM with marked decreases in mast cell burden and improved patient symptoms
- Data support the hypothesis that KIT D816V is a key disease driver in SM
- Half-life > 19 hours supports QD dosing
- BLU-285 has been well tolerated over a dose range of 30 to 100 mg - dose escalation (currently at 130 mg QD)
- BLU-285 deserves continued investigation in advanced SM, and further investigation in other KIT-driven diseases; Phase 1 study of BLU-285 in GIST is ongoing

GIST, gastrointestinal stromal tumor

Study sponsored by Blueprint Medicines Corporation

Acknowledgments

- This study was sponsored by Blueprint Medicines
- We thank the participating patients, their families, all study co-investigators, and research coordinators at the following institutions:

  - Guy's & St Thomas NHS Trust
  - Gartnavel General Hospital, Beatson West of Scotland Cancer Center
  - Abramson Cancer Center at the University of Pennsylvania
  - University of Michigan Comprehensive Cancer Center
  - Dana-Farber Cancer Institute
  - University of Utah, Huntsman Cancer Institute
  - MD Anderson Cancer Center
  - University of Colorado
  - Stanford University

Study sponsored by Blueprint Medicines Corporation

Permissions

- **Slide 3 images:**
  - **Blood, Bone and Bone Marrow**

Republished with permission of American Society of Hematology, from Mast Cells and mastocytosis, Dean D Metcalfe, volume 112, number 4, 2008

  - **Skin**

Reprinted from Journal of Allergy and Clinical Immunology, Volume 137, Issue 1, Hartmann et al., Cutaneous manifestations in patients with mastocytosis: Consensus report of the European Competence Network on Mastocytosis; the American Academy of Allergy, Asthma, and Immunology; and the European Academy of Allergology and Clinical Immunology, pages 35–45, 2016, with permission from Elsevier

  - **Liver and spleen**

Annals of Hematology, Isolated splenomegaly as the only presentation of systemic mastocytosis, 92, 2013, pg. 1574 Figure 1, Nischala Ammannagari, Sara Grethlein, James J. Longhi, and John M. Fisk, Copyright Springer-Verlag Berlin Heidelberg 2013, With permission from Springer

  - **GI tract**

Reprinted from Behdad A, Owens SR. Systemic Mastocytosis Involving the Gastrointestinal Tract: Case Report and Review. Arch Pathol Lab Med. 2013; 137(9):1220-1223 with permission from *Archives of Pathology & Laboratory Medicine*. Copyright 2013. College of American Pathologists