

**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 5, 2016**

Blueprint Medicines Corporation

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-37359
(Commission File Number)

26-3632015
(I.R.S. Employer
Identification No.)

38 Sidney Street, Suite 200
Cambridge, Massachusetts
(Address of principal executive offices)

02139
(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 7.01 Regulation FD Disclosure.

On December 5, 2016, Blueprint Medicines Corporation hosted an investor conference call and live webcast to discuss initial data from the dose escalation stage of its ongoing Phase 1 clinical trial evaluating BLU-285 for the treatment of advanced systemic mastocytosis. These data were presented in an oral presentation at the 2016 American Society of Hematology Annual Meeting and Exposition in San Diego, California on December 4, 2016. BLU-285 is an orally available, potent and highly selective inhibitor that targets D816V mutant KIT. A copy of the slide presentation from the conference call is attached as Exhibit 99.1 to this Current Report on Form 8-K.

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1 attached hereto, 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.

<u>Exhibit No.</u>	<u>Description</u>
99.1	Slide presentation by Blueprint Medicines Corporation on December 5, 2016

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	Slide presentation by Blueprint Medicines Corporation on December 5, 2016



**2016 American Society of Hematology (ASH) Annual Meeting
San Diego, CA**

Summary of BLU-285 Systemic Mastocytosis Oral Presentation

Blueprint Medicines Corporation
Investor Webcast & Conference Call

December 5, 2016



Jeff Albers
Chief Executive Officer, Blueprint Medicines



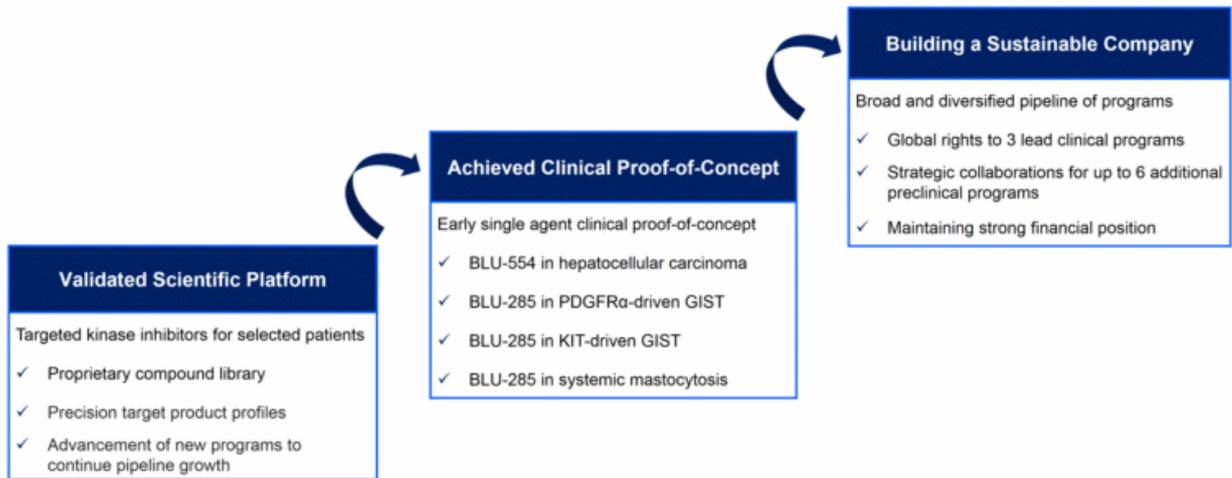
Andy Boral, M.D.
Chief Medical Officer, Blueprint Medicines

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 about plans and timelines for the clinical development of BLU-285, BLU-554 and BLU-667 and our ability to implement those clinical development plans; the potential benefits of our current and future drug candidates in treating patients; the timing of regulatory submissions or filings; plans and timelines for the development of companion diagnostics for BLU-285 and BLU-554; plans and timelines for current or future discovery programs; the future financial performance of Blueprint Medicines Corporation (the "Company"); and the Company's strategy, 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 future clinical trials or the development of the Company's drug candidates, including BLU-285, BLU-554 and BLU-667; the Company's advancement of multiple early-stage efforts; the Company's ability to successfully demonstrate the efficacy and safety of its drug candidates; 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 current or future 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 diagnostics for its current and future drug candidates, including a companion diagnostic for BLU-554 with Ventana Medical Systems, Inc. and a companion diagnostic for BLU-285 with QIAGEN Manchester Limited; 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 under "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 any other filings the Company 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 the date hereof, 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.



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 Drummond¹, Daniel DeAngelo², Michael Deininger³, Deepti Radia⁴,
Albert Quiery⁵, Elizabeth Hexner⁶, Hongliang Shi⁷, Terri Alvarez-Diez⁷,
Erica Evans⁷, Mary Ellen Healy⁷, Beni Wolf⁷, Srdan Verstovsek⁸

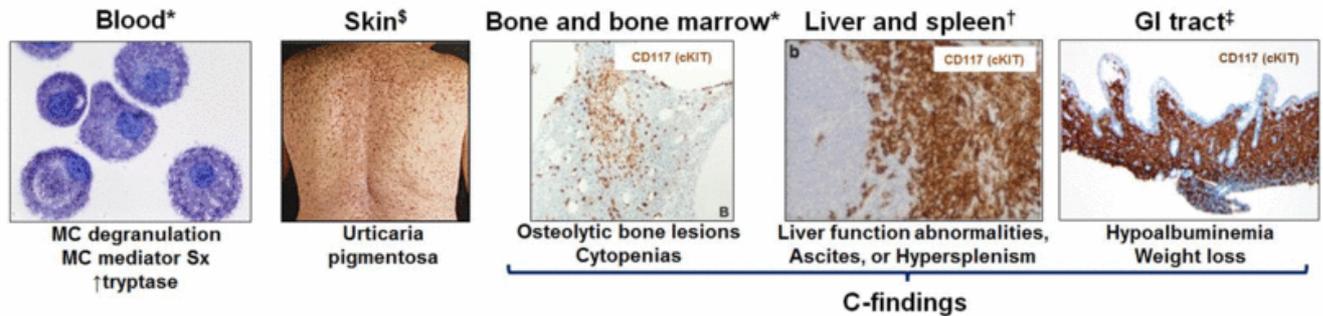
¹Beatson West of Scotland Cancer Centre, NHS Greater Glasgow and Clyde, Glasgow, United Kingdom;
²Dana-Farber Cancer Institute, Boston, MA; ³Division of Hematology and Hematologic Malignancies,
Huntsman Cancer Institute, The University of Utah, Salt Lake City, UT; ⁴Guy's & St Thomas NHS Trust,
London, United Kingdom; ⁵University of Michigan, Ann Arbor, MI; ⁶Abramson Cancer Center of the
University of Pennsylvania, Philadelphia, PA; ⁷Blueprint Medicines, Cambridge, MA; ⁸Department 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 patients¹

Mast cell accumulation and organ infiltration



MC, mast cell; MCL, mast cell leukemia; SM, systemic mastocytosis; C- findings, clinical findings

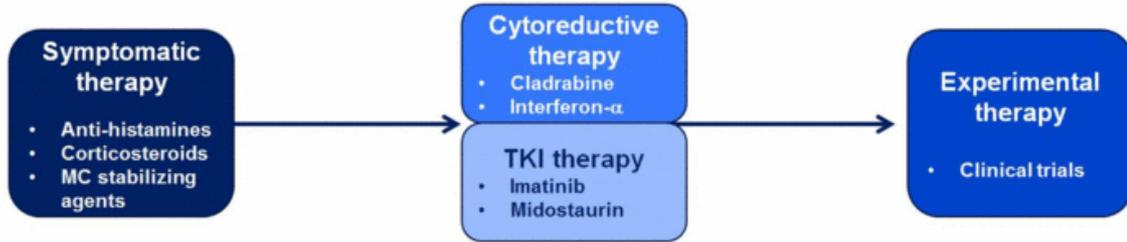
[§]Garcia-Montero AC et al (2006)

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

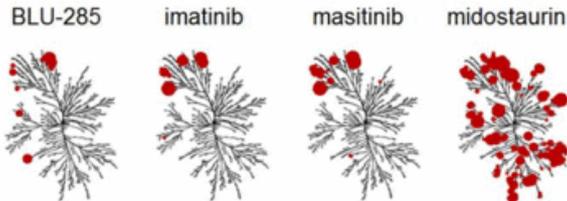
¹Lim KH et al (2009)

- ↓Life expectancy with current therapy¹
- Morbidity via C-findings
 - Cytopenias
 - Osteolytic bone lesions
 - Hepatomegaly with liver dysfunction
 - Hypersplenism
 - Malabsorption with weight loss

BLU-285: Potent, Highly Selective KIT D816V Inhibition

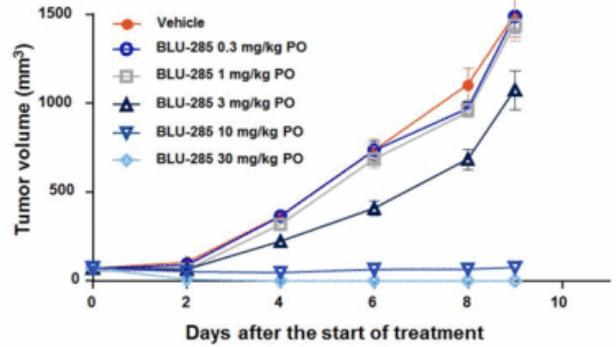
Biochemical profiles

	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



IC₅₀, half maximal inhibitory concentration; K_D, dissociation constant; PO, orally
 *Evans E et al (2014)
 Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com)

Anti-tumor activity in KIT-driven mastocytoma model¹



Model driven by KIT mutation equivalent to human KIT D816 mutation

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 $\geq 25 \times 10^9$ /L
- ANC $\geq 0.5 \times 10^9$ /L
- Adequate hepatic and renal function

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

BLU-285 Phase 1 Objectives and Design

Enrolling

3 + 3 dose escalation

- MTD and safety profile
- PK, PD, anti-neoplastic activity
- D816V allele burden

Advanced SM

FPI March 2016

MTD

Dose expansion

- Response rate per IWG-MRT-ECNM criteria¹
- D816V allele burden
- Advanced SM- PRO

ASM, N = 15

SM-AHN, N = 15

MCL, N = 5

BLU-285 continuous once-daily oral dosing

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
¹Gottib J et al (2013); NCT02561988

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)
Urticaria Pigmentosa / Other SM-related skin rash, n (%)	8 (67)

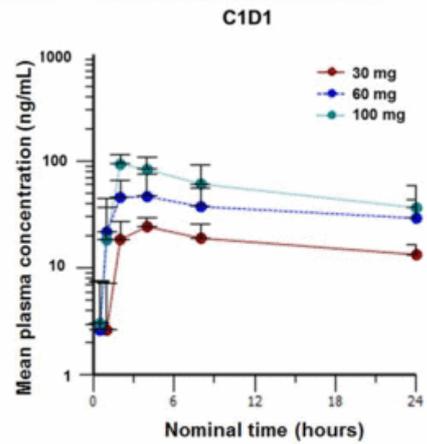
SM-CMML, systemic mastocytosis with chronic myelomonocytic leukemia; pt, patient

¹One pt had no detectable KIT D816V mutation in blood or bone marrow; ²2 pts had midostaurin; 1 pt 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	



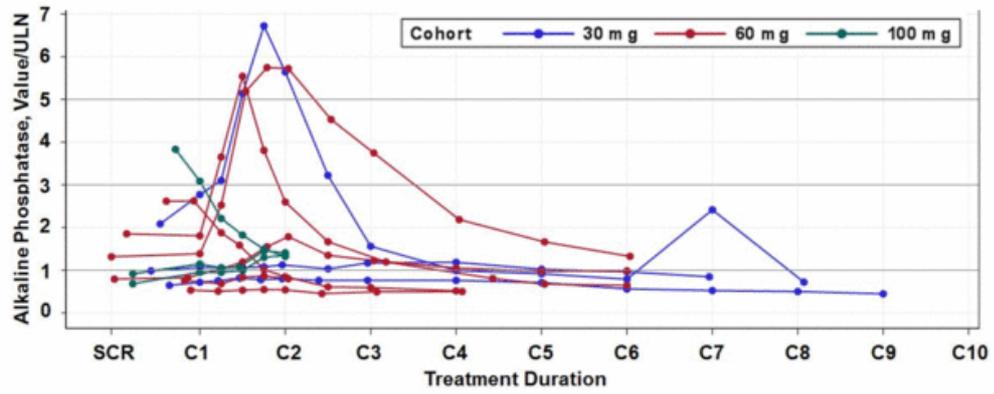
- Dose-dependent increase in exposure
- Rapid absorption: t_{max} 2–4 hours
- Half-life > 19 hours supports QD dosing

Adverse Events

Non-hematological adverse events ≥ 2 patients (safety population, N = 12)			Hematological adverse events (safety population, N = 12)		
Adverse event	Any grade n (%)	Grade 3 n (%)	Adverse event	Any grade n (%)	Grade 3 n (%)
Fatigue	4 (33)	0	Anemia	3 (25)	0
↑ Alkaline Phosphatase	3 (25)	3 (25)	Thrombocytopenia	2 (17)	1 (8)
Diarrhea	2 (17)	0	Neutropenia	0	0
Dizziness	2 (17)	0			
Headache	2 (17)	0			
Nausea	2 (17)	0			
Pruritus	2 (17)	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

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

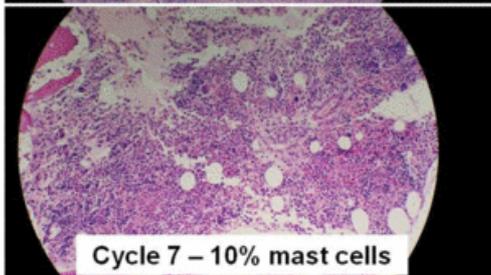
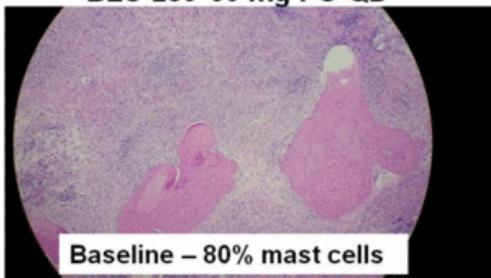


- Asymptomatic, transient Grade 3 alkaline phosphatase elevation occurred in the 3 patients with highest baseline bone marrow (BM) MC burden
- No associated transaminase or bilirubin elevation
- Confirmed bone origin in 1 patient (2 others not assessed)
- May represent a PD effect on BM MCs
- Protocol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

BLU-285 Markedly Reduces Bone Marrow Mast Cells

Aggressive Systemic Mastocytosis

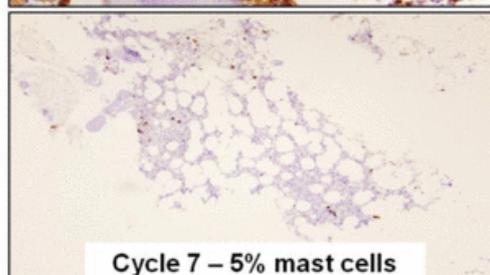
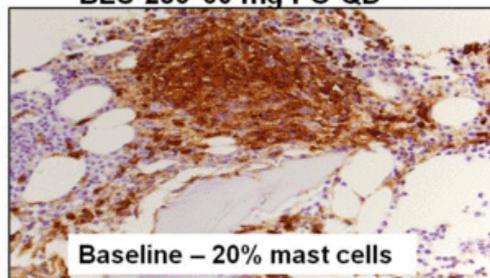
BLU-285 30 mg PO QD



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

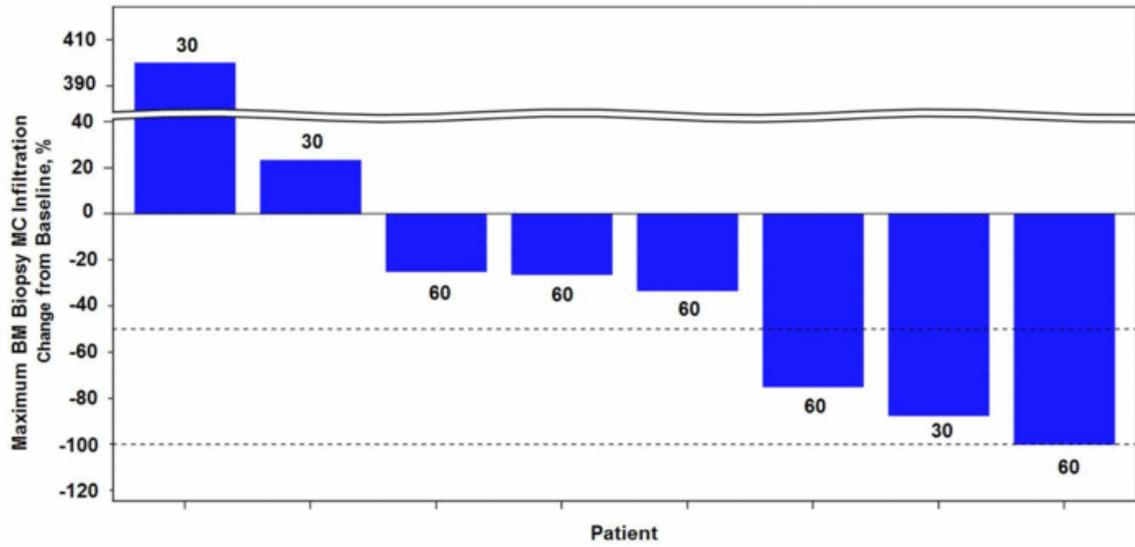
Aggressive Systemic Mastocytosis

BLU-285 60 mg PO QD*



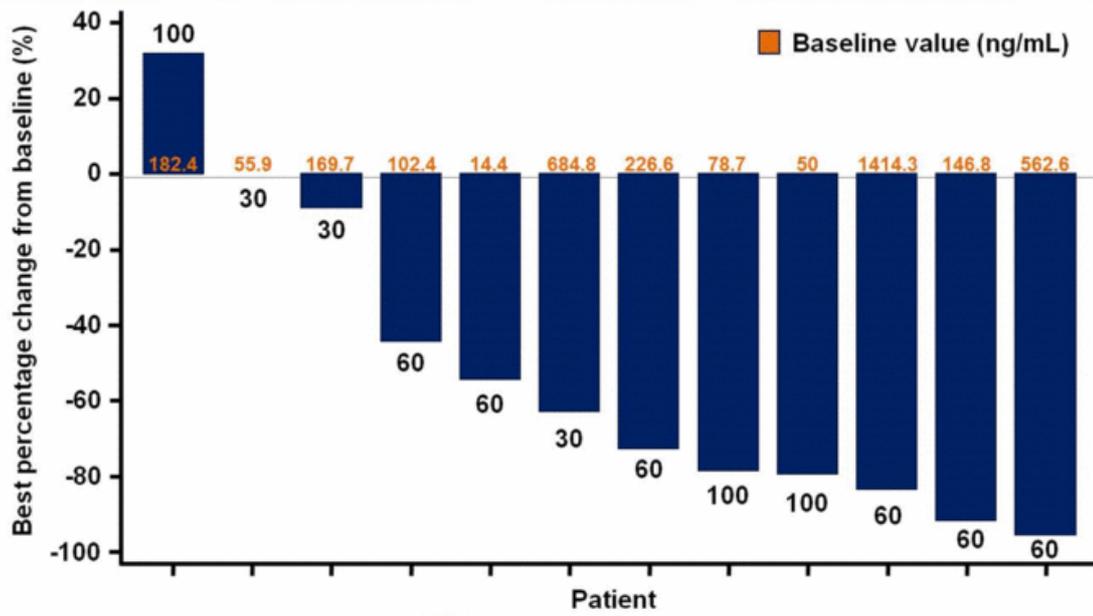
Study sponsored by Blueprint Medicines Corporation

Decreased BM Mast Cells 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

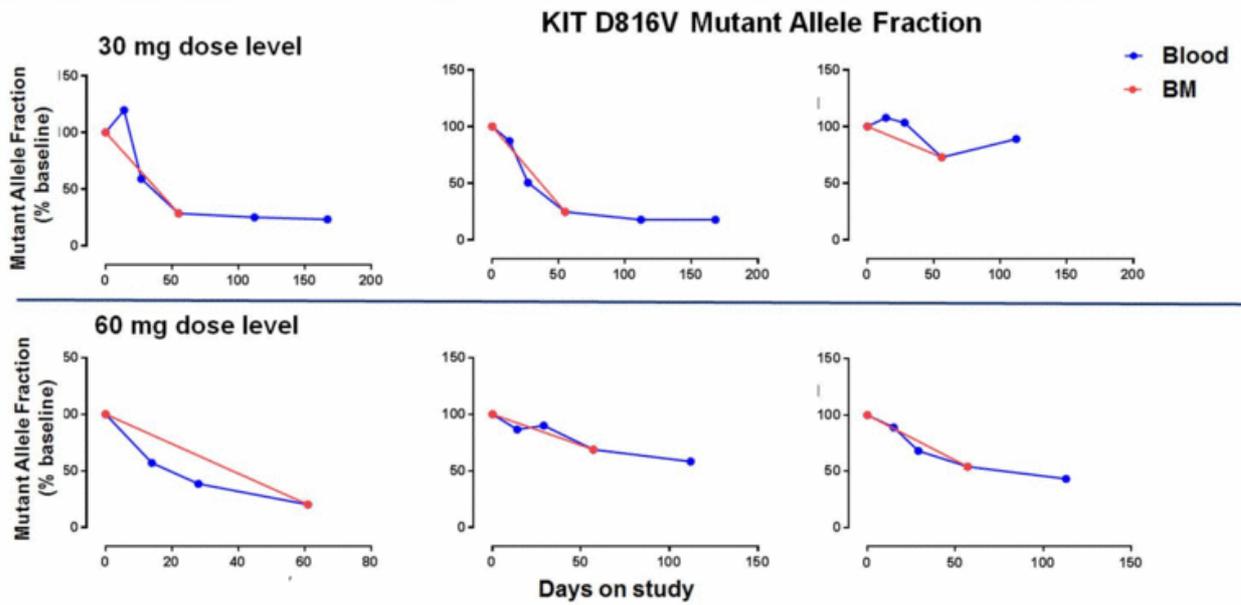
Decreased Tryptase in 10 of 12 Patients



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



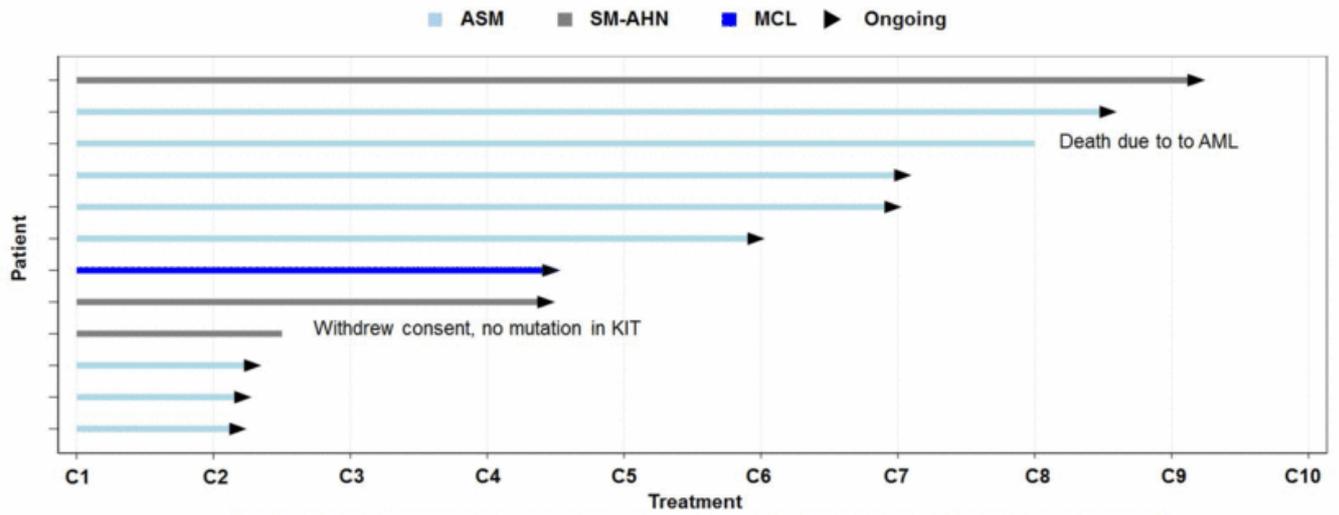
All available data as of data cutoff date shown

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 Urticaria Pigmentosa for whom data are available

BLU-285 Duration on Study



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

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

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

Robust Portfolio with Diverse Clinical Stage Assets

Initial Diseases	Discovery	Pre-Clinical	Clinical Development	Commercial Rights
GIST PDGFRα D842V and KIT Exon 17 Mutations	BLU-285		Phase 1	
HCC FGFR4 Inhibitor	BLU-554		Phase 1	
SM KIT D816V Mutations	BLU-285		Phase 1	
NSCLC, Thyroid RET Fusions & Resistant Mutants	BLU-667			
FLC (Fibrolamellar Carcinoma) PRKACA Fusions				
Cancer Immunotherapy Immunokinases	Up to 5 Programs			
Rare Genetic Disease	Target and Development Stage Undisclosed			

*NTRK inhibitor program is not represented on this slide.

Systemic Mastocytosis

- Continue dose escalation to define an MTD and to maximize clinical activity in advanced SM patients
- Initiate expansion upon definition of a recommended dose to evaluate the potential of BLU-285 as a single agent in advanced SM
- Accelerate the evaluation of expanded development options, including opportunities for development in indolent SM and KIT-driven acute myeloid leukemia

GIST

- Continue dose escalation to define an MTD and to maximize clinical activity in KIT-driven patients
- Increase the cohort sizes in the expansion to evaluate the potential of BLU-285 as a single agent therapy in PDGFR α -driven and KIT-driven GIST
- Seek guidance from the FDA on the development path forward, including any possibilities for expedited clinical development of BLU-285 for the treatment of advanced GIST
- Accelerate the evaluation of expanded development options, including opportunities to move to earlier lines of therapy and possible combinations

HCC

- Continue enrollment in the expansion to define the patient population(s), based on their biomarker status, that may respond to BLU-554 as a single agent therapy
- Accelerate the evaluation of expanded development options, including opportunities to move to earlier lines of therapy and possible combinations



Questions & Answers
