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 10, 2017**

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:

- o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- o 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. ☑

Item 7.01 Regulation FD Disclosure.

On December 10, 2017, Blueprint Medicines Corporation (the "Company") issued a press release announcing new data from its ongoing Phase 1 clinical trial evaluating avapritinib (formerly known as BLU-285) for the treatment of advanced systemic mastocytosis. The data were presented on Sunday, December 10, 2017 in an oral presentation during the plenary session at the American Society of Hematology ("ASH") Annual Meeting in Atlanta, Georgia. 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 11, 2017, the Company hosted an investor conference call and live webcast to discuss the data presented at the ASH Annual Meeting and provide a corporate update. A copy of the presentation from the conference call 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 10, 2017
99.2	Presentation by Blueprint Medicines Corporation at the ASH Annual Meeting on December 10, 2017
99.3	Presentation by Blueprint Medicines Corporation at investor conference call on December 11, 2017

EXHIBIT INDEX

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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 11, 2017

By: /s/ Tracey L. McCain
Tracey L. McCain
Chief Legal Officer

Blueprint Medicines Announces New Data from Ongoing Phase 1 Clinical Trial of Avapritinib (BLU-285) in Patients with Advanced Systemic Mastocytosis Showing Evidence of Strong Clinical Activity

– Overall Response Rate of 72 Percent and Disease Control Rate of 100 Percent Reported –
– Plan to Engage Global Regulatory Authorities in First Half 2018 on Registration Pathway –
– Blueprint Medicines to Host Investor Conference Call and Webcast on Monday, December 11, at 6:00 a.m. ET –

CAMBRIDGE, Mass., December 10, 2017 – Blueprint Medicines Corporation (NASDAQ:BPMC), a leader in discovering and developing targeted kinase medicines for patients with genomically defined diseases, today announced new data from its ongoing Phase 1 clinical trial of avapritinib (formerly known as BLU-285), a potent and highly selective KIT and PDGFRα inhibitor in development for patients with advanced systemic mastocytosis (SM). The new data from the dose escalation portion of the Phase 1 trial showed strong clinical activity regardless of advanced SM subtype, prior treatment with midostaurin or the presence of additional mutations.

As of the data cutoff date of October 4, 2017, the data showed an overall response rate (ORR) of 72 percent and a disease control rate (DCR) of 100 percent in patients evaluable for response, based on the International Working Group-Myeloproliferative Neoplasms Research and Treatment and European Competence Network on Mastocytosis (IWG-MRT-ECNM) consensus criteria. As of the data cutoff date, avapritinib was well-tolerated and most adverse events (AEs) reported by investigators were Grade 1 or 2. In addition, there were no discontinuations due to treatment-related adverse events, and 30 of 32 patients remained on treatment with a median treatment duration of nine months. The data will be presented today in an oral presentation during the Plenary Scientific Session at the 59th American Society of Hematology Annual Meeting and Exposition (ASH) in Atlanta, Georgia.

Based on these data, Blueprint Medicines plans to engage global regulatory authorities in the first half of 2018 to obtain input on registration pathways for avapritinib in patients with advanced SM and patients with indolent and smoldering SM. Subject to regulatory feedback, the Company anticipates initiating a registration-enabling clinical trial of avapritinib in patients with advanced SM in the first half of 2018 and a dose escalation and proof-of-concept clinical trial of avapritinib in patients with indolent and smoldering SM in the second half of 2018. In addition, Blueprint Medicines continues to enroll patients in the expansion portion of the ongoing Phase 1 clinical trial in patients with advanced SM with the goal of generating additional data in 2018.

“The new clinical trial results for avapritinib reported at the ASH plenary scientific session represent an exciting milestone for the systemic mastocytosis community. The data showed a remarkably high response rate and a favorable tolerability profile, suggesting avapritinib has the potential to transform the treatment of this devastating rare disease,” said Daniel J. DeAngelo, M.D., Ph.D., Director of Clinical and Translational Research, Adult Leukemia at Dana-Farber Cancer Institute, Associate Professor of Medicine at Harvard Medical School, and an investigator on the Phase 1 trial. “The data also provide strong evidence that selective inhibition of D816V mutant KIT, a disease-driver present in nearly all patients across the spectrum of SM, is a potentially important treatment strategy that may offer patients improved outcomes. These data strongly support continued development of avapritinib in a broad population of patients with SM.”

“We are extremely encouraged by the tolerability and clinical activity of avapritinib observed to date, which increase our confidence and reinforce our commitment to rapidly advance its development across the spectrum of SM,” said Andy Boral, M.D., Ph.D., Chief Medical Officer at Blueprint Medicines. “We look forward to engaging with global regulatory authorities in the first half of 2018 to obtain feedback on a potential registration pathway. In addition, based on data showing a favorable tolerability profile and strong clinical activity from the lowest dose levels tested, we plan to expand our clinical development program to address the full spectrum of SM, including advanced, smoldering and indolent forms of the disease, over the course of 2018.”

New Data from the Ongoing Phase 1 Clinical Trial of Avapritinib in Advanced SM

As of the data cutoff date of October 4, 2017, 32 patients had been treated with avapritinib in the dose escalation portion of the Phase 1 clinical trial at seven dose levels (ranging from 30 mg to 400 mg once daily (QD)), including 17 patients with aggressive SM (ASM), nine patients with advanced SM with an associated hematologic neoplasm (SM-AHN) and three patients with mast cell leukemia (MCL). The KIT D816V mutation was confirmed in 28 patients. Overall, 22 patients (69 percent) previously received anti-neoplastic therapy, including four patients (13 percent) who previously received midostaurin.

Based on pharmacokinetic (PK) data, avapritinib demonstrated a mean half-life of greater than 20 hours, supporting a QD dosing regimen.

Blueprint Medicines has selected 300 mg QD as the recommended part two dose (RP2D) for the expansion portion of this trial, which was initiated in the second quarter of 2017. A maximum tolerated dose of avapritinib in advanced SM was not determined.

Safety Data

As of the data cutoff date, avapritinib was generally well-tolerated. Most AEs reported by investigators were Grade 1 or 2. The most common treatment-emergent AEs reported by investigators (≥20 percent) across all grades included periorbital edema (59 percent), fatigue (41 percent), peripheral edema (34 percent), nausea (28 percent), anemia (28 percent), thrombocytopenia (28 percent), abdominal pain, diarrhea, respiratory tract infection, dizziness and headache (22 percent each). Investigators reported treatment-related Grade ≥3 AEs in 16 patients (50 percent), with only one treatment-related Grade ≥3 AE occurring in more than 10 percent of patients (neutropenia, 13 percent).

No patients discontinued treatment due to a treatment-related AE. Two patients discontinued treatment with avapritinib, including one patient with ASM who had progressive disease with transformation to acute myeloid leukemia and one patient with SM-AHN and no identified KIT mutation (i.e., wild-type KIT). Overall, 30 of 32 patients enrolled in the dose escalation portion of the trial remained on treatment as of the data cutoff date, with a median duration of 9 months (range 4 to 19 months).

Clinical Activity Data

IWG-MRT-ECNM Response Assessment

The IWG-MRT-ECNM criteria comprise a rigorous assessment of clinical response in patients with advanced SM. These criteria include objective measures of bone marrow mast cell burden, serum tryptase and improvement in organ damage as measured by a clinical improvement (CI) finding.

As of the data cutoff date, 18 patients had advanced SM and were evaluable for response by the IWG-MRT-ECNM criteria.

Across all 18 evaluable patients with advanced SM, the data showed an ORR of 72 percent and a complete response (CR) + partial response (PR) rate of 56 percent. A detailed summary of response data is provided below.

Avapritinib in Patients with Advanced SM; Assessment of Response per IWG-MRT-ECNM Criteria				
*Best Response, Number of Patients (%)**	*ASM (n=7)*	*SM-AHN (n=8)*	*MCL (n=3)*	*Overall (n=18)*
CR	2 (29%)	0	0	2 (11%)
PR	3 (43%)	4 (50%)	1 (33%)	8 (44%)
Clinical improvement (CI)	1 (14%)	1 (13%)	1 (33%)	3 (17%)
Stable disease (SD)	1 (14%)	3 (38%)	1 (33%)	5 (28%)
ORR (CR + PR + CI)	6 (86%)	5 (63%)	2 (67%)	13 (72%)
CR + PR	5 (71%)	4 (50%)	1 (33%)	10 (56%)

**Responses pending confirmation: ASM: 2 CR; SM-AHN: 3 PR*

Additional Clinical Assessments

In addition, results from individual components of the IWG-MRT-ECNM were reported as of the data cutoff date. Clinically meaningful improvements were observed in all evaluable patients, across all subtypes of advanced SM and at all avapritinib dose levels evaluated.

- All 32 enrolled patients had decreases in serum tryptase greater than 50 percent.
- All 25 patients who had bone marrow mast cell infiltrate of at least 5 percent at baseline (measured by bone marrow biopsy) showed decreases in bone marrow mast cell burden. In this group, 21 patients had at least a 50 percent decrease, and 15 patients achieved a CR for bone marrow mast cell burden.
- All 25 patients with centrally reviewed radiographic scans showed decreases in spleen volume. In this group, 14 patients had at least a 35 percent reduction in spleen volume.

In addition, rash improved in 13 of 15 patients with urticaria pigmentosa at baseline, based on investigator assessments. Urticaria pigmentosa is an allergy-mediated rash common in SM patients.

Conference Call Information

Blueprint Medicines will host a conference call and webcast on Monday, December 11, 2017 at 6:00 a.m. ET to discuss the avapritinib (BLU-285) clinical data presented at ASH and provide an update on its broader preclinical and clinical pipeline.

To participate in the conference call, please dial 1-855-728-4793 (domestic) or 1-503-343-6666 (international) and refer to conference ID 4072589. A live webcast will be available under "Events and Presentations" in the Investors section of Blueprint Medicines' website at http://ir.blueprintmedicines.com. A replay of the webcast will be available approximately two hours after the conference call and will be available for 30 days following the call.

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

The Phase 1 clinical trial of avapritinib is designed to evaluate the safety and tolerability of avapritinib in adults with advanced SM. The trial consists of two parts, a dose escalation portion and an expansion portion. The dose escalation portion is complete, and Blueprint Medicines selected 300 mg QD as the RP2D for the dose expansion portion of the trial. The expansion portion is actively enrolling patients in three defined cohorts for specific subtypes of advanced SM, including ASM, SM-AHN and MCL. Trial objectives include assessing safety and tolerability, response per IWG-MRT-ECNM criteria and additional clinical outcome measures of mast cell burden, organ function and disease symptoms. The Phase 1 clinical trial is designed to enroll approximately 60 patients, including approximately 35 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, smoldering SM and more advanced forms of SM, which include ASM, SM-AHN and MCL. SM is a hematological clonal disorder 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 ASM, SM-AHN and MCL, mast cell infiltration in bone marrow, liver and other vital organs can eventually lead to organ dysfunction and shortened life expectancy, with a median overall survival of three to five years. Patients with indolent SM do not have a shortened life expectancy, but they do suffer from a broad range of acute and chronic symptoms that negatively impact their quality of life. There are no approved treatments that target D816V mutant KIT, 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 Avapritinib (BLU-285)

Avapritinib is an orally available, potent and highly selective inhibitor of KIT and PDGFRα. Preclinical data have shown that avapritinib is active across a broad spectrum of KIT and PDGFRα mutations, including KIT D816V, PDGFRα D842V and KIT exon 17 mutations for which there are limited or no effective treatment options. Blueprint Medicines is initially developing avapritinib, an investigational medicine, for the treatment of patients with advanced gastrointestinal stromal tumors (GIST) and advanced SM. Avapritinib was discovered by Blueprint Medicines' research team leveraging its proprietary compound library, and the Company retains worldwide development and commercialization rights for avapritinib.

In June 2017, avapritinib received Breakthrough Therapy Designation from the U.S. Food and Drug Administration (FDA) for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRα D842V mutation. The FDA's Breakthrough Therapy Designation is intended to expedite the development and review of a drug candidate intended to treat a serious or life-threatening disease or condition, when preliminary clinical evidence indicates that the drug candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Previously, the FDA granted orphan drug designation to avapritinib for the treatment of GIST and mastocytosis. The FDA also granted Fast Track designation to avapritinib for the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second tyrosine kinase inhibitor and for the treatment of patients with unresectable or metastatic GIST in patients with the PDGFRα D842V mutation regardless of prior therapy. In addition, the European Commission has granted orphan drug designation to avapritinib for the treatment of GIST.

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 four programs in clinical development for subsets of patients with gastrointestinal stromal tumors, hepatocellular carcinoma, systemic mastocytosis, non-small cell lung cancer, medullary thyroid cancer and other advanced solid tumors, as well as multiple programs in research and preclinical development. For more information, please visit www.blueprintmedicines.com.

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 avapritinib (formerly known as BLU-285), including plans and timelines for initiating a registration-enabling clinical trial for avapritinib in patients with advanced SM and a dose escalation and proof-of-

concept clinical trial for avapritinib in patients with indolent and smoldering SM; Blueprint Medicines' ability to implement its clinical development plans for avapritinib in advanced SM; expectations regarding current and future interactions with global regulatory authorities, including the FDA, and the impact of Breakthrough Therapy Designation on the development of avapritinib; 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 candidates, including BLU-285, BLU-554 and BLU-667; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' ability to successfully demonstrate the safety and efficacy of its drug candidates; the preclinical and clinical results for Blueprint Medicines' drug candidates, which may not support further development of such drug 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 diagnostic tests for its current and future drug candidates, including companion diagnostic tests for BLU-554 for FGFR4-driven HCC, BLU-285 for PDGFRα D842V-driven GIST and BLU-667 for RET-driven non-small cell lung cancer; and the success of Blueprint Medicines' 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, 2017, as filed with the Securities and Exchange Commission (SEC) on October 31, 2017, 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.

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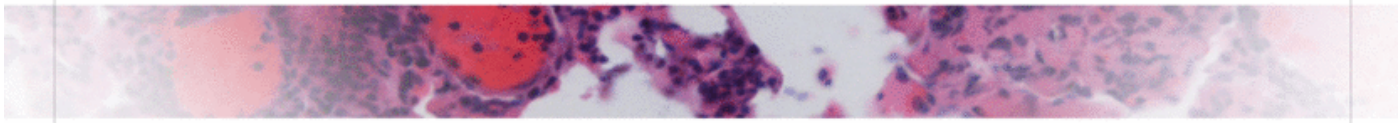
American Society *of* Hematology
Helping hematologists conquer blood diseases worldwide



Clinical activity in a Phase 1 study of BLU-285, a potent, highly-selective inhibitor of KIT D816V in advanced systemic mastocytosis

Daniel J. DeAngelo, Albert T. Quiery, Deepti Radia, Mark W. Drummond, Jason Gotlib, William A. Robinson, Elizabeth Hexner, Srdan Verstovsek, Hongliang Shi, Terri Alvarez-Diez, Oleg Schmidt-Kittler, Erica Evans, Mary E. Healy, Beni B. Wolf and Michael W. Deininger

American Society of Hematology Annual Meeting, Atlanta, GA USA,10 Dec 2017

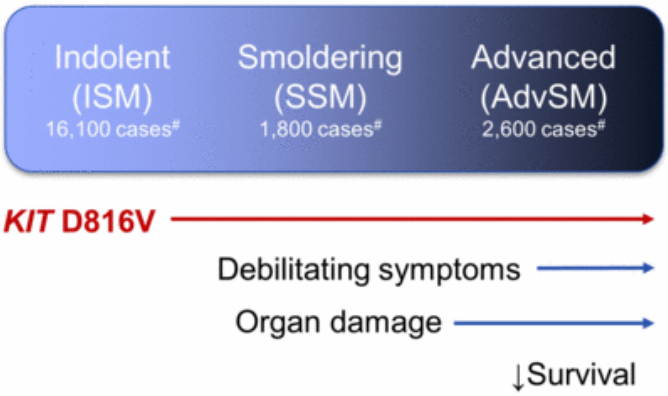
Systemic mastocytosis (SM)

***Diagnostic Criteria for* systemic mastocytosis[1]**

WHO Criteria

- **Major (+1 minor)**
  - Mast cell aggregates (≥ 15) in BM or other tissue
- **Minor (or 3 of 4)**
  - Spindle-shaped mast cells
  - c-KIT D816V mutation present
  - CD2 or CD25 expression on mast cells
  - Serum tryptase > 20 ng/mL

***KIT* D816V drives systemic mastocytosis[2–3]**



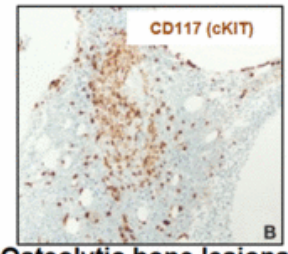
#Represents estimated prevalence in US, EU5, Japan. WHO, World Health Organization; AdvSM, advanced SM; ISM, indolent SM; SSM, smoldering SM

1. Arber DA, et al. Blood. 2016:127(20):2391-2405; 2. Valent P et al Cancer Res (2017) 77:1261; 3. Cohen S et al Br J Haematol (2014) 166(4):521-8 and World Bank Population estimates

Systemic mastocytosis (SM)

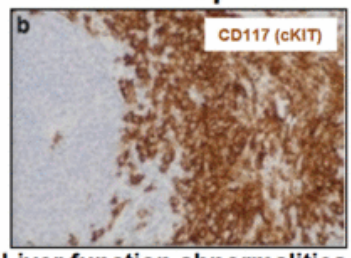
Advanced systemic mastocytosis
ASM, SM-AHN and MCL

Bone and bone marrow*



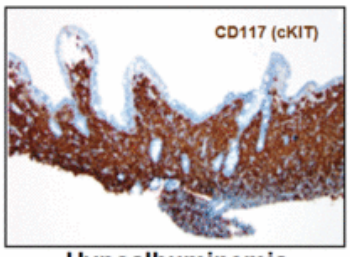
Osteolytic bone lesions
Cytopenias

Liver and spleen†



Liver function abnormalities,
Ascites, or Hypersplenism

GI tract‡



Hypoalbuminemia
Weight loss

C-findings

*Represents estimated prevalence in US, EU5, Japan. AdvSM, advanced SM; ASM, aggressive systemic mastocytosis; GI, gastrointestinal; ISM, indolent SM; MC, mast cell; MCL, mast cell leukemia; SM-AHN, SM-associated hematologic neoplasm; SSM, smoldering SM. Images reproduced with permission from: *Metcalfe Blood (2008) 112:4; †Ammanagari N et al Ann Hematol (2013) 92:1573–1575; ‡Behdad A., Owens SR Arch Pathol Lab Med (2013) 137:1220–1223; §Hartmann K et al Journal of Allergy and Clinical Immunology (2016) 137 (1) 35–45

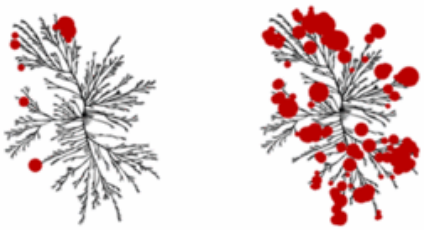
BLU-285 was designed to treat systemic mastocytosis

BLU-285 provides highly potent and selective targeting of KIT D816V[1]

Biochemical IC_{50} (nM)

	KIT D816V	KIT wild type
BLU-285	0.27	73
Midostaurin	2.9	26

Kinome selectivity*



BLU-285 Midostaurin

- Multikinase inhibitor midostaurin is the only approved treatment for AdvSM
- Midostaurin provides CR+PR of 17% per IWG-MRT-ECNM criteria;[2] mPFS 14.1 months[3]

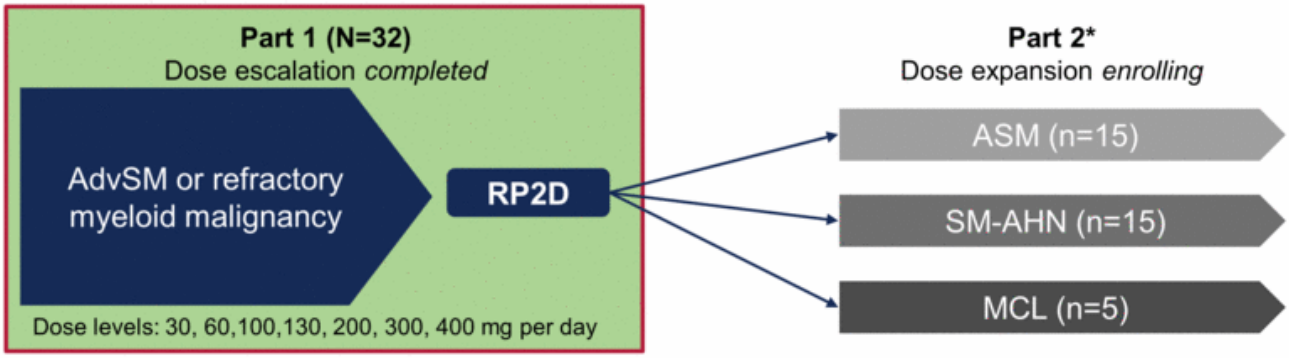
*Reproduced courtesy of Cell Signalling Technology, Inc. (www.cellsignal.com). The website is maintained by CSTI, Blueprint Medicines is not responsible for its content. IC_{50}, concentration causing 50% inhibition; CR, complete response; PR, partial response; IWG-MRT-ECNM, International Working Group-Myeloproliferative Neoplasms Research and Treatment & European Competence Network on Mastocytosis; mPFS, median progression free survival

1. Evans E et al Science Translational Medicine (2017) 1;9(414);
2. Midostaurin US Prescribing information;
3. Gotlib J et al NEJM (2016) 374:2530

Phase 1 study of BLU-285 in advanced systemic mastocytosis: study design

Primary objectives: MTD/RP2D and safety profile

Secondary objectives: pharmacokinetics and preliminary anti-tumor activity



BLU-285 continuous oral once-daily dosing

*As of November 27, 2017, 7 patients have been enrolled in dose expansion (data not shown); MTD, maximum tolerated dose; RP2D, recommended Part 2 dose

Key entry criteria

- Disease entities:
  - Advanced systemic mastocytosis per *WHO diagnostic criteria* via local assessment:
    - One of the following three histologic subtypes:
      - Aggressive systemic mastocytosis
      - Systemic mastocytosis with associated hematologic neoplasm with ≥1 C-finding
      - Mast cell leukemia
  - Relapsed or refractory myeloid malignancy (dose escalation only)
- Age ≥18 years
- ECOG performance status 0–3
- Platelet count ≥ 25 x 10^9 /L
- ANC ≥ 0.5 x 10^9 /L
- Adequate hepatic and renal function

***WHO* Criteria for SM**

- **Major**
  - Mast cell aggregates (≥ 15) in BM or other tissue
- **Minor**
  - Spindle-shaped mast cells
  - c-KIT D816V mutation present
  - CD2 or CD25 expression on mast cells
  - Serum tryptase > 20 ng/mL

ANC, absolute neutrophil count; ECOG, Eastern Cooperative Oncology Group.

Baseline characteristics

Parameter		All patients (N=32)
Median age, years (range)		63 (34–83)
Disease subtype per local assessment, n (%)*	ASM SM-AHN MCL	17 (53) 9 (28) 3 (9)
KIT mutation, n (%)	D816V	28 (88)
High risk mutation positive,[1,2] n (%)	Any (*SRSF2*, *ASXL1* or *RUNX1*)#	14 (44)
ECOG performance status, n (%)	0-1 2	27 (84) 5 (16)
Prior anti-neoplastic therapy	Median number (range) Any, n (%) Midostaurin	1 (0-2) 22^ (69) 4 (13)
C-findings per WHO Criteria	Median number (range) Cytopenias, n (%) Hepatomegaly with liver dysfunction Hypersplenism Malabsorption with weight loss Osteolytic bone lesions	1 (0–4) 17 (53) 5 (16) 11 (34) 9 (28) 6 (19)

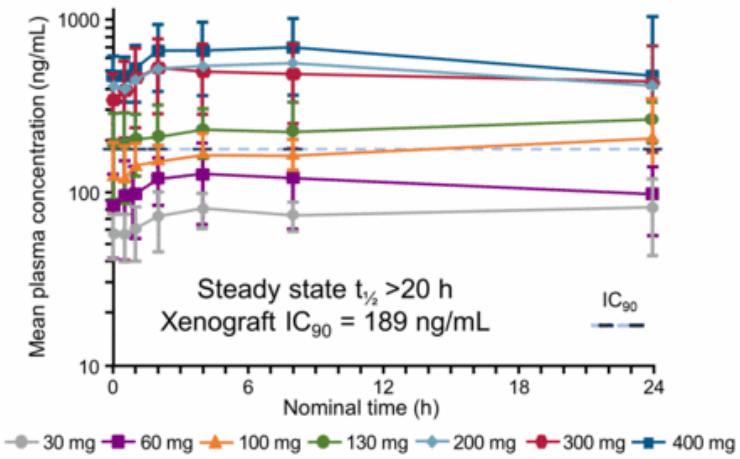
*Other, SSM (n=2); telangiectasia macularis eruptive perstans (n=1); # Patients could have more than one S/A/R gene mutated, *SFSR2 (n=22), ASXL1 (n=7), RUNX1 (n=5)*. S/A/R, mutations potentially associated with a poorer prognosis[1,2]; ^ Prior therapy taken by ≥2 pts, cladribine (n=6), imatinib (n=4), interferon (n=4), midostaurin (n=4), azacitidine (n=3), hydroxyurea (n=2), ibrutinib (n=2)

Data cut-off: 4 Oct 2017

1. Schwaab J et al Blood (2013) 122:2460;
2. Jawhar M et al Blood (2017) 130:137

BLU-285 pharmacokinetics (PK) and dose escalation cohorts

Steady state PK



PK support QD dosing

3+3 dose escalation with enrichment

Dose (mg)	Patients (n)	DLT (n)
30	3	0
60	6	1 Grade 3 alk phos
100	3	0
130	3	0
200	4	0
300	6	0
400	7	1 Grade 4 vomiting

MTD not reached

300 mg daily selected as the RP2D

QD, once daily; DLT, dose-limiting toxicity

Treatment-emergent adverse events

NON-HEMATOLOGICAL AEs ≥20% (N=32)

Adverse event, n (%)	Any grade	≥Grade 3
Periorbital edema	19 (59)	2 (6)
Fatigue	13 (41)	2 (6)
Peripheral edema	11 (34)	0
Nausea	9 (28)	1 (3)
Abdominal pain	7 (22)	0
Diarrhea	7 (22)	1 (3)
Respiratory tract infection	7 (22)	0
Dizziness	7 (22)	0
Headache	7 (22)	0
HEMATOLOGICAL AEs ≥10% (N=32)		
Anemia	9 (28)	3 (9)
Thrombocytopenia	9 (28)	2 (6)
Neutropenia	4 (13)	4 (13)

Most adverse events were CTCAE grade 1 or 2

≥ Grade 3 treatment-related AE in 16 (50%) patients
No deaths on study

30 of 32 patients remain on treatment (Median 9 months [range: 4–19])

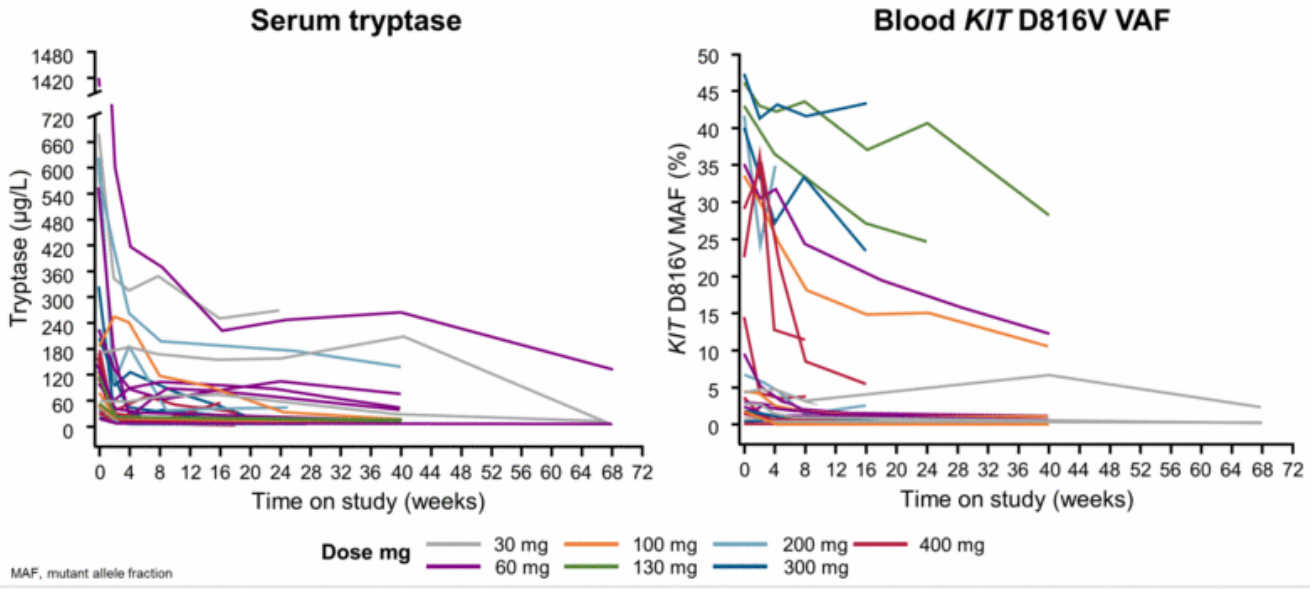
1 discontinued due to PD (AML)

1 investigator decision (wild type *KIT*)

None discontinued due to BLU-285-related AE

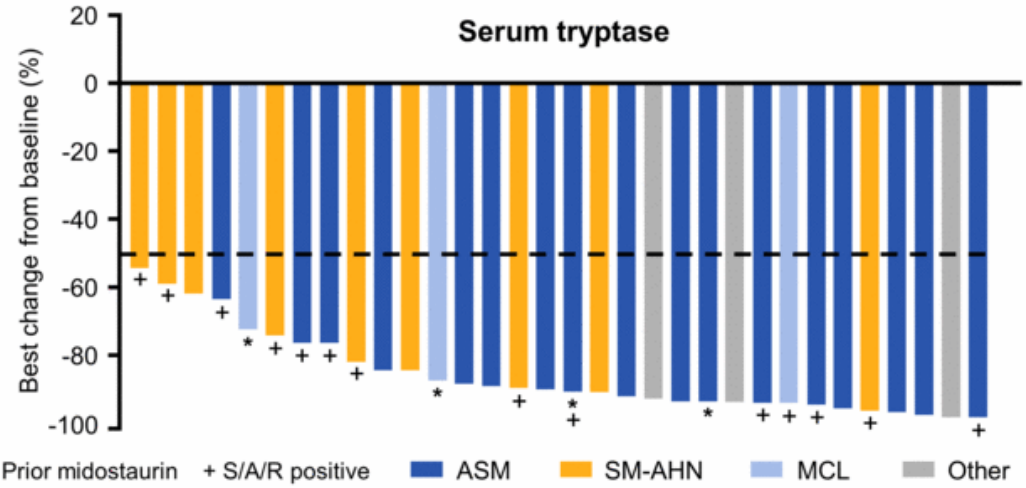
AE, adverse event; AML, acute myeloid leukemia; CTCAE, Common Terminology Criteria for Adverse Events; PD, progressive disease

Rapid and durable decline in tryptase and *KIT* D816V variant allele fraction across all dose levels



MAF, mutant allele fraction

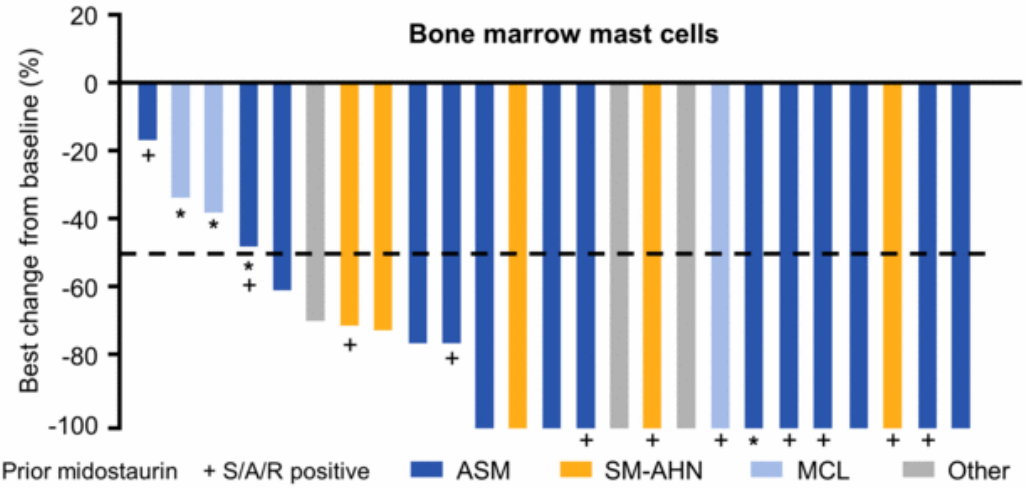
Tryptase decrease in all patients



- Baseline median 124 µg/L, range 14 to 1414 µg/L
- All 32 patients achieved >50% reduction from baseline

Other, SSM (n=2); telangiectasia macularis eruptive perstans (n=1)

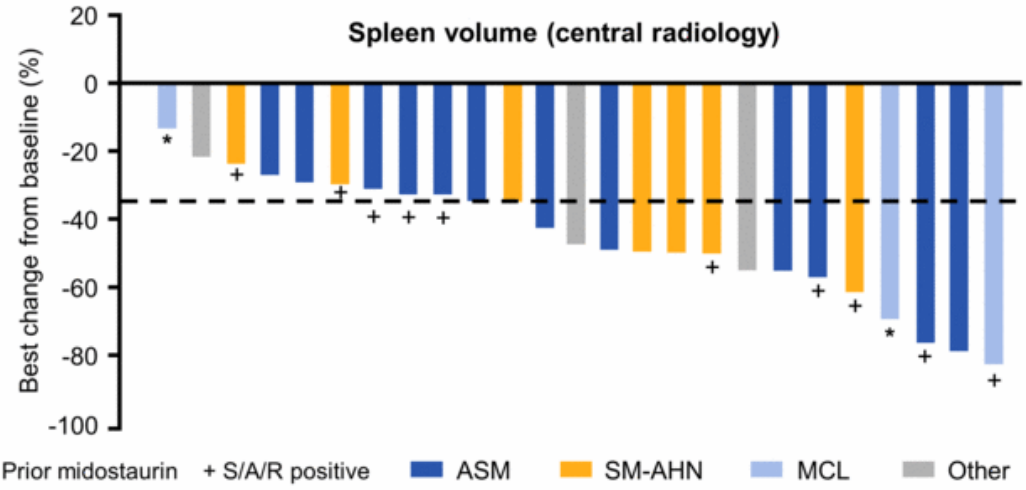
Bone marrow mast cell decrease in all patients^



- Baseline median 20%, range 1.5 to 95%
- ^n=25 evaluable patients with baseline bone marrow mast cells ≥ 5%
- 15/25 (60%) patients achieved bone marrow CR

Other, SSM (n=2); telangiectasia macularis eruptive perstans (n=1)

Spleen volume decrease in all patients^



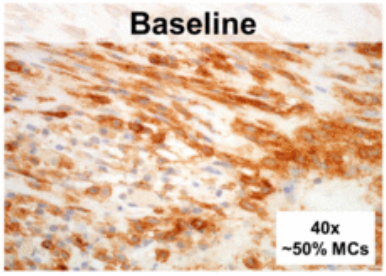
* Prior midostaurin + S/A/R positive ASM SM-AHN MCL Other

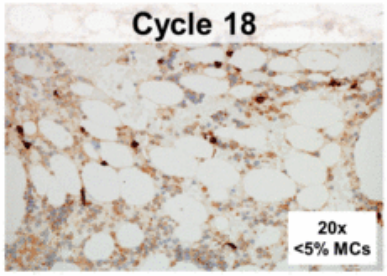
- Baseline median 633 mL, range 130 to 1952 mL
- ^n=25 patients with splenomegaly as per central assessment
- 15/25 (60%) patients achieved >35% reduction of spleen volume

Other, SSM (n=2); telangiectasia macularis eruptive perstans (n=1)

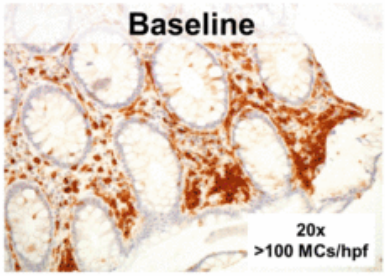
45-year-old female with ASM

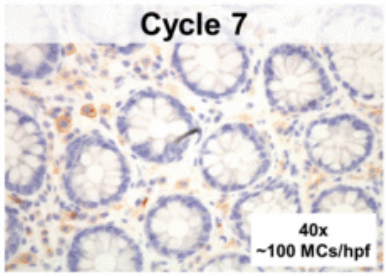
Bone marrow tryptase





Colon CD25



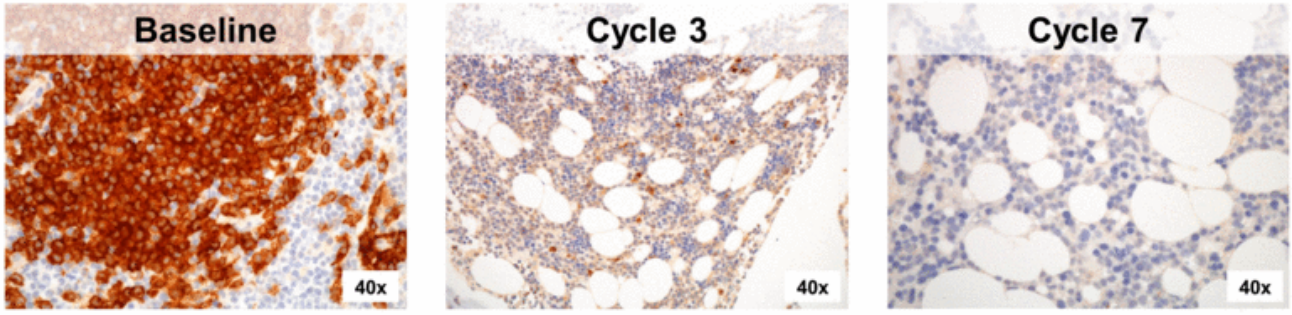


*BLU-285 60 mg; remains on treatment at cycle 18 with confirmed PR per IWG-MRT-ECNM

Images courtesy of Dr Deepti Radia, Guy's and St. Thomas NHS Trust

64-year-old male with MCL

Progressive clearance of bone marrow mast cells



Bone marrow CD117

*BLU-285 200 mg; remains on treatment at cycle 9 with confirmed PR per IWG-MRT-ECNM

Images courtesy of Dr Deepti Radia, Guy's and St. Thomas NHS Trust

Response analysis per IWG-MRT-ECNM criteria

Complete response (CR)[1]

- No bone marrow mast cell aggregate
- Serum tryptase <20 ng/mL
- Peripheral blood count remission
- Complete resolution of C-findings

Partial response (PR)[1]

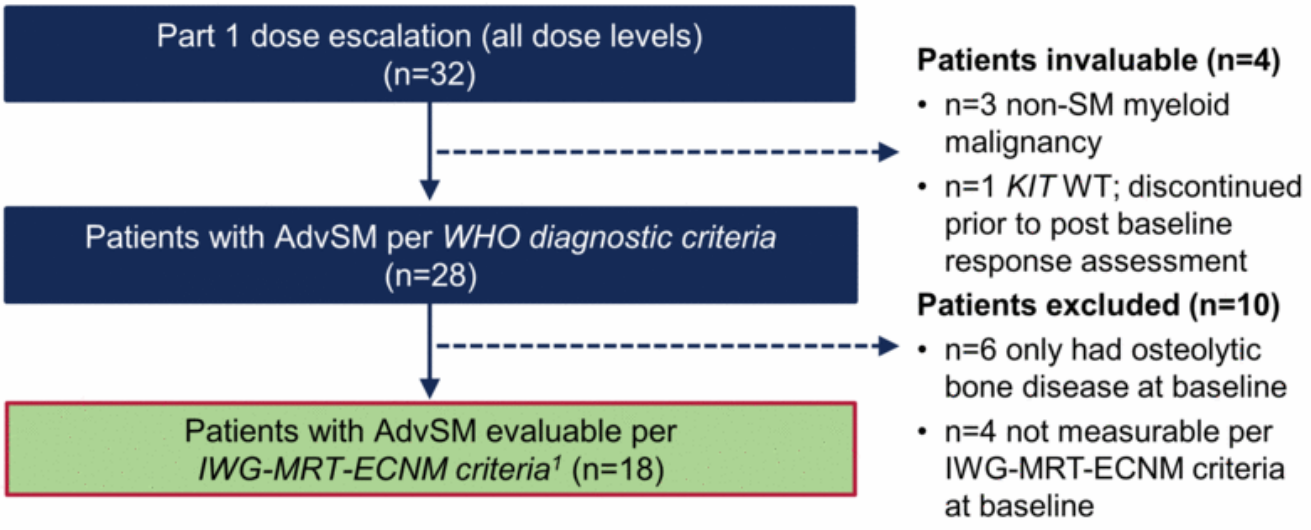
- ≥50% reduction in bone marrow mast cell aggregate
- ≥50% reduction in serum tryptase
- Resolution of 1 or more C-findings

Clinical improvement (CI)[1]

- 1 or more response criteria in absence of CR, PR or PD

[1]Gotlib, et al. Blood. 2013 Mar 28; 121(13): 2393–2401

IWG-MRT-ECNM evaluable patients



WT, wild type; 1. Gotlib J et al Blood (2013) 121:2393

Best overall response per IWG-MRT-ECNM criteria[1]

Best response* n (%) (confirmed and unconfirmed)	ASM (n=7)	SM-AHN# (n=8)	MCL (n=3)	Overall (n=18)
Overall response rate (CR + PR + CI)	6 (86)	5 (63)	2 (67)	13 (72)
CR + PR	5 (71)	4 (50)	1 (33)	10 (56)
Complete response (CR)	2 (29)	0	0	2 (11)
Partial response (PR)	3 (43)	4 (50)	1 (33)	8 (44)
Clinical improvement (CI)	1 (14)	1 (13)	1 (33)	3 (17)
Stable disease (SD)	1 (14)	3 (38)	1 (33)	5 (28)
Progressive disease (PD)	0	0	0	0

- 17 of 18 patients remain on treatment with median duration 9 months (range: 4–19)

*Pending confirmation: ASM, 2 CR; SM-AHN, 3 PR; #Mastocytosis response; 1. Gotlib J et al Blood (2013) 121:2393

BLU-285 has potent, clinically important activity in AdvSM

- Data validate *KIT* D816V as a key disease driver
- Selective targeting of *KIT* D816V with BLU-285 is well tolerated
  - 30 of 32 patients remain on treatment with median duration of 9 months (range: 4–19)
  - RP2D is 300 mg once daily, and expansion is ongoing
- BLU-285 demonstrates high preliminary response rates and durable activity
  - 72% ORR (CR + PR + CI) with 56% CR + PR per IWG-MRT-ECNM criteria
- Additional clinical development with BLU-285, now avapritinib, across the spectrum of systemic mastocytosis is planned for 2018
  - Phase 2 trial in AdvSM
  - Dose finding and Phase 2 trial in ISM and SSM

Acknowledgments

- We thank the participating patients, their families, all study co-investigators, and research coordinators at the following institutions:
  - Deepti Radia, Guy's & St Thomas NHS Trust
  - Mark Drummond, Beatson West of Scotland Cancer Centre
  - Elizabeth Hexner, Abramson Cancer Center at the University of Pennsylvania
  - Albert Quiery, University of Michigan Comprehensive Cancer Center
  - Dan DeAngelo, Dana-Farber Cancer Institute
  - Michael Deininger, University of Utah, Huntsman Cancer Institute
  - Srdan Verstovsek, MD Anderson Cancer Center
  - William Robinson, University of Colorado
  - Jason Gotlib, Stanford Cancer Institute
- We thank Tracy George, Hans Peter Horny, and Maureen Conlan for expert technical analyses
- We also thank Sarah Jackson, PhD, of iMed Comms, an Ashfield company, who provided editorial writing support funded by Blueprint Medicines


blueprint MEDICINES
BLU-285
in Advanced
Systemic Mastocytosis
MONDAY, DECEMBER 11, 2017

Conference call participants

Jeff Albers
Chief Executive Officer, Blueprint Medicines

Andy Boral, MD, PhD
Chief Medical Officer, Blueprint Medicines

Daniel J. DeAngelo, MD, PhD
Director, Clinical and Translational Research, Adult Leukemia, Dana-Farber Cancer Institute
Associate Professor of Medicine, Harvard Medical School

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 about plans and timelines for the clinical development of avapritinib (formerly known as BLU-285), BLU-554 and BLU-667 and the ability of Blueprint Medicines Corporation (the "Company") to implement those clinical development plans; the potential benefits of the Company's current and future drug candidates in treating patients; plans and timelines for regulatory submissions, filings or discussions; plans and timelines for the development and commercialization of companion diagnostics for the Company's current or future drug candidates; plans and timelines for current or future discovery programs; plans and timelines for any current or future collaborations with strategic partners; expectations regarding the Company's existing cash, cash equivalents and investments or the future financial performance of the Company; expectations regarding potential milestones; 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 planned clinical trials or the development of Company's drug candidates, including avapritinib, BLU-554 and BLU-667; Company's advancement of multiple early-stage efforts; Company's ability to successfully demonstrate the efficacy and safety of its drug candidates; the preclinical and clinical results for Company's drug candidates, which may not support further development of such drug candidates; and actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; Company's ability to develop and commercialize companion diagnostic tests for its current and future drug candidates, including companion diagnostic tests for BLU-554 for FGFR4-driven HCC, avapritinib for PDGFRα D842V-driven GIST and BLU-667 for RET-driven non-small cell lung cancer; and the success of Company's 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, 2017, as filed with the Securities and Exchange Commission ("SEC") on October 31, 2017, 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 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.

Welcome

Jeff Albers, Chief Executive Officer

Avapritinib (formerly BLU-285) is a pipeline within a single investigational medicine

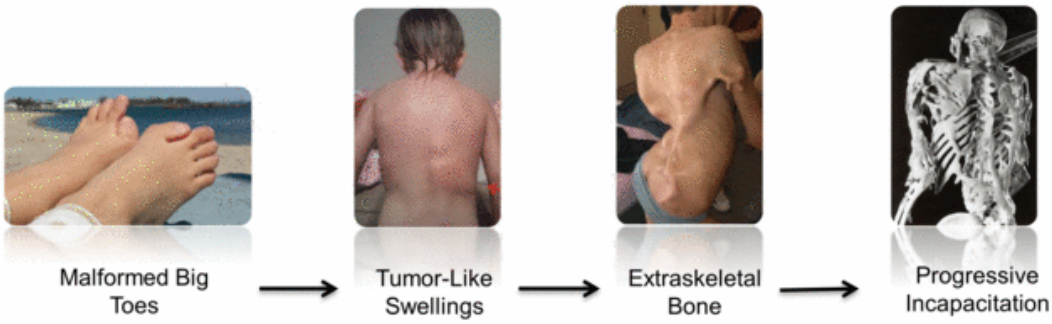
blueprint MEDICINES

Active development Planned development Future potential opportunity

Update on Phase 1 clinical trial of BLU-667 in RET-altered cancers

- Initiated Phase 1 clinical trial of BLU-667 in patients with RET-altered non-small cell lung cancer (NSCLC), medullary thyroid cancer (MTC) and other advanced solid tumors in Q1 2017
- Enrollment progressing well at multiple clinical sites
- As of December 1, 2017:
  - 30 patients have been enrolled in dose escalation, with enrollment ongoing
  - BLU-667 has been generally well-tolerated
    - Majority of adverse events reported by investigators were Grade 1
    - Maximum tolerated dose and recommended part 2 dose have not been identified
  - Preliminary evidence of clinical activity observed in patients with NSCLC (including KIF5B and other RET fusions) and RET-altered MTC
- Plan to present preliminary clinical data in 1H 2018
- Plan to initiate expansion portion of Phase 1 trial in 1H 2018

BLU-782 selected as development candidate for potential treatment of fibrodysplasia ossificans progressiva



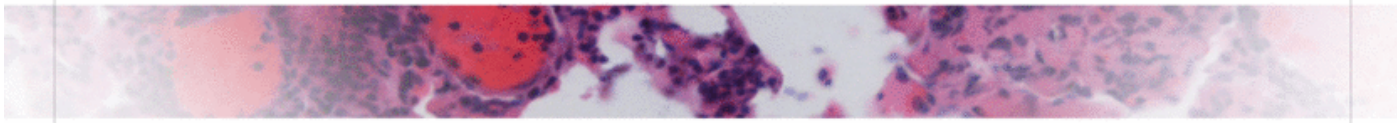
- Devastating, ultra-rare genetic disease caused by mutations in the ALK2 gene, ACVR1
- Characterized by abnormal transformation of skeletal muscle, ligaments and tendons into bone
- Progressive loss of mobility and respiratory function, with median age of death of ~40 years
- Blueprint Medicines' differentiated approach targets underlying cause of disease
- Plan to initiate IND-enabling studies in 1H 2018

Robust pipeline of diverse clinical and preclinical stage assets

DRUG CANDIDATE	DISCOVERY	PRECLINICAL	CLINICAL	COMMERCIAL RIGHTS
avapritinib (BLU-285) Inhibitor of KIT and PDGFRα			REGISTRATION-ENABLING TRIAL – PDGFRα-DRIVEN GIST PHASE 1 – KIT-DRIVEN GIST PHASE 1 – SYSTEMIC MASTOCYTOSIS	
BLU-554 Inhibitor of FGFR4			PHASE 1 – HEPATOCELLULAR CARCINOMA	
BLU-667 Inhibitor of RET			PHASE 1 – NSCLC, THYROID & OTHER CANCERS[1]	
BLU-782 Inhibitor of ALK2			FIBRODYSPLASIA OSSIFICANS PROGRESSIVA	
2 undisclosed kinase targets				
Cancer immunotherapy Immunokinases			UP TO 5 PROGRAMS, TARGET AND DEVELOPMENT STAGE UNDISCLOSED[2]	Roche

[1] Phase 1 trial includes a basket cohort that consists of other advanced solid tumors with RET alterations.
[2] Blueprint Medicines has U.S. commercial rights for up to two programs. Roche has worldwide commercialization rights for up to three programs and ex-U.S. commercialization rights for up to two programs.
All Phase 1 clinical trials are in advanced disease.

American Society of Hematology
Helping hematologists conquer blood diseases worldwide



Clinical activity in a Phase 1 study of BLU-285, a potent, highly-selective inhibitor of KIT D816V in advanced systemic mastocytosis

Daniel J. DeAngelo, Albert T. Quiery, Deepti Radia, Mark W. Drummond, Jason Gotlib, William A. Robinson, Elizabeth Hexner, Srdan Verstovsek, Hongliang Shi, Terri Alvarez-Diez, Oleg Schmidt-Kittler, Erica Evans, Mary E. Healy, Beni B. Wolf and Michael W. Deininger

American Society of Hematology Annual Meeting, Atlanta, GA USA,10 Dec 2017

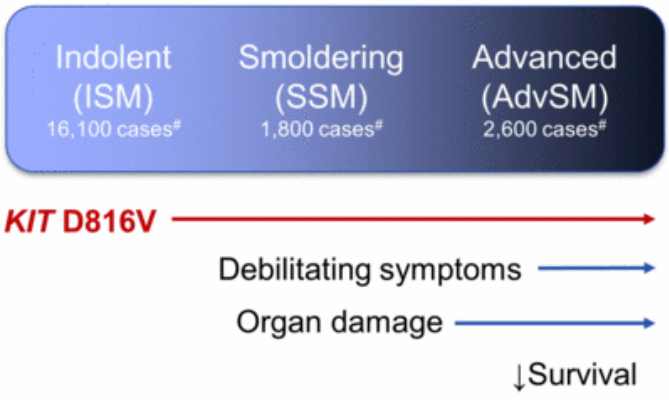
Systemic mastocytosis (SM)

***Diagnostic Criteria for* systemic mastocytosis[1]**

WHO Criteria

- **Major (+1 minor)**
  - Mast cell aggregates (≥ 15) in BM or other tissue
- **Minor (or 3 of 4)**
  - Spindle-shaped mast cells
  - c-KIT D816V mutation present
  - CD2 or CD25 expression on mast cells
  - Serum tryptase > 20 ng/mL

***KIT* D816V drives systemic mastocytosis[2–3]**



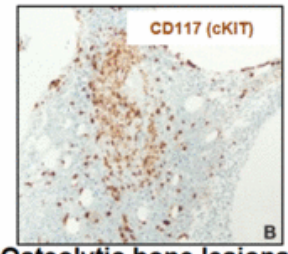
#Represents estimated prevalence in US, EU5, Japan. WHO, World Health Organization; AdvSM, advanced SM; ISM, indolent SM; SSM, smoldering SM

1. Arber DA, et al. Blood. 2016:127(20):2391-2405; 2. Valent P et al Cancer Res (2017) 77:1261; 3. Cohen S et al Br J Haematol (2014) 166(4):521-8 and World Bank Population estimates

Systemic mastocytosis (SM)

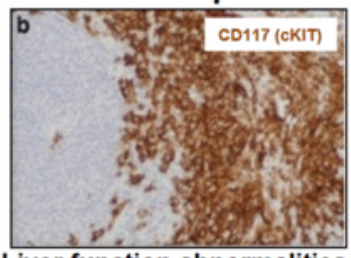
Advanced systemic mastocytosis
ASM, SM-AHN and MCL

Bone and bone marrow*



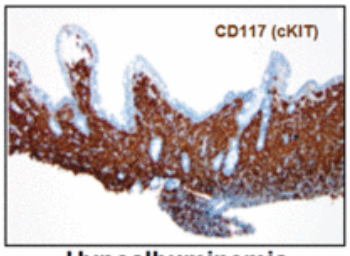
Osteolytic bone lesions
Cytopenias

Liver and spleen†



Liver function abnormalities,
Ascites, or Hypersplenism

GI tract‡



Hypoalbuminemia
Weight loss

C-findings

*Represents estimated prevalence in US, EU5, Japan. AdvSM, advanced SM; ASM, aggressive systemic mastocytosis; GI, gastrointestinal; ISM, indolent SM; MC, mast cell; MCL, mast cell leukemia; SM-AHN, SM-associated hematologic neoplasm; SSM, smoldering SM. Images reproduced with permission from: *Metcalfe Blood (2008) 112:4; †Ammanagari N et al Ann Hematol (2013) 92:1573–1575; ‡Behdad A., Owens SR Arch Pathol Lab Med (2013) 137:1220–1223; §Hartmann K et al Journal of Allergy and Clinical Immunology (2016) 137 (1) 35–45

BLU-285 was designed to treat systemic mastocytosis

BLU-285 provides highly potent and selective targeting of KIT D816V[1]

Biochemical IC_{50} (nM)

	KIT D816V	KIT wild type
BLU-285	0.27	73
Midostaurin	2.9	26

Kinome selectivity*

BLU-285 Midostaurin

- Multikinase inhibitor midostaurin is the only approved treatment for AdvSM
- Midostaurin provides CR+PR of 17% per IWG-MRT-ECNM criteria;[2] mPFS 14.1 months[3]

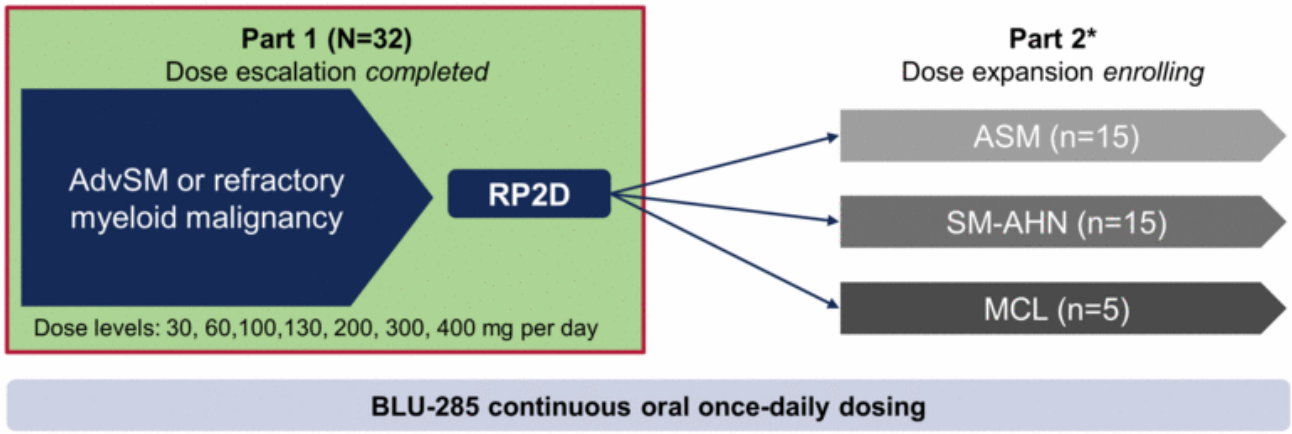
*Reproduced courtesy of Cell Signalling Technology, Inc. (www.cellsignal.com). The website is maintained by CSTI, Blueprint Medicines is not responsible for its content. IC_{50}, concentration causing 50% inhibition; CR, complete response; PR, partial response; IWG-MRT-ECNM, International Working Group-Myeloproliferative Neoplasms Research and Treatment & European Competence Network on Mastocytosis; mPFS, median progression free survival

1. Evans E et al Science Translational Medicine (2017) 1;9(414);
2. Midostaurin US Prescribing information;
3. Gotlib J et al NEJM (2016) 374:2530

Phase 1 study of BLU-285 in advanced systemic mastocytosis: study design

Primary objectives: MTD/RP2D and safety profile

Secondary objectives: pharmacokinetics and preliminary anti-tumor activity



BLU-285 continuous oral once-daily dosing

*As of November 27, 2017, 7 patients have been enrolled in dose expansion (data not shown); MTD, maximum tolerated dose; RP2D, recommended Part 2 dose

Key entry criteria

- Disease entities:
  - Advanced systemic mastocytosis per *WHO diagnostic criteria* via local assessment:
    - One of the following three histologic subtypes:
      - Aggressive systemic mastocytosis
      - Systemic mastocytosis with associated hematologic neoplasm with ≥1 C-finding
      - Mast cell leukemia
  - Relapsed or refractory myeloid malignancy (dose escalation only)
- Age ≥18 years
- ECOG performance status 0–3
- Platelet count ≥ 25 x 10^9 /L
- ANC ≥ 0.5 x 10^9 /L
- Adequate hepatic and renal function

***WHO* Criteria for SM**

- **Major**
  - Mast cell aggregates (≥ 15) in BM or other tissue
- **Minor**
  - Spindle-shaped mast cells
  - c-KIT D816V mutation present
  - CD2 or CD25 expression on mast cells
  - Serum tryptase > 20 ng/mL

ANC, absolute neutrophil count; ECOG, Eastern Cooperative Oncology Group.

Baseline characteristics

Parameter		All patients (N=32)
Median age, years (range)		63 (34–83)
Disease subtype per local assessment, n (%)*	ASM SM-AHN MCL	17 (53) 9 (28) 3 (9)
KIT mutation, n (%)	D816V	28 (88)
High risk mutation positive,[1,2] n (%)	Any (*SRSF2*, *ASXL1* or *RUNX1*)#	14 (44)
ECOG performance status, n (%)	0-1 2	27 (84) 5 (16)
Prior anti-neoplastic therapy	Median number (range) Any, n (%) Midostaurin	1 (0-2) 22^ (69) 4 (13)
C-findings per WHO Criteria	Median number (range) Cytopenias, n (%) Hepatomegaly with liver dysfunction Hypersplenism Malabsorption with weight loss Osteolytic bone lesions	1 (0–4) 17 (53) 5 (16) 11 (34) 9 (28) 6 (19)

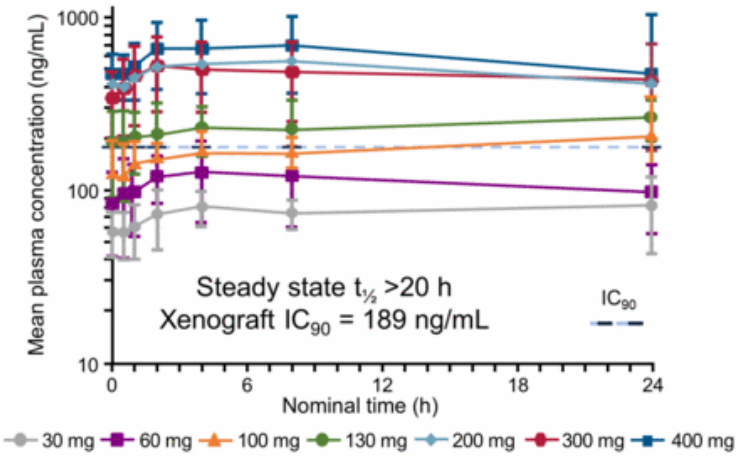
*Other, SSM (n=2); telangiectasia macularis eruptive perstans (n=1); # Patients could have more than one S/A/R gene mutated, *SFSR2 (n=22), ASXL1 (n=7), RUNX1 (n=5)*. S/A/R, mutations potentially associated with a poorer prognosis[1,2]; ^ Prior therapy taken by ≥2 pts, cladribine (n=6), imatinib (n=4), interferon (n=4), midostaurin (n=4), azacitidine (n=3), hydroxyurea (n=2), ibrutinib (n=2)

Data cut-off: 4 Oct 2017

1. Schwaab J et al Blood (2013) 122:2460;
2. Jawhar M et al Blood (2017) 130:137

BLU-285 pharmacokinetics (PK) and dose escalation cohorts

Steady state PK



PK support QD dosing

3+3 dose escalation with enrichment

Dose (mg)	Patients (n)	DLT (n)
30	3	0
60	6	1 Grade 3 alk phos
100	3	0
130	3	0
200	4	0
300	6	0
400	7	1 Grade 4 vomiting

MTD not reached

300 mg daily selected as the RP2D

QD, once daily; DLT, dose-limiting toxicity

Treatment-emergent adverse events

NON-HEMATOLOGICAL AEs ≥20% (N=32)

Adverse event, n (%)	Any grade	≥Grade 3
Periorbital edema	19 (59)	2 (6)
Fatigue	13 (41)	2 (6)
Peripheral edema	11 (34)	0
Nausea	9 (28)	1 (3)
Abdominal pain	7 (22)	0
Diarrhea	7 (22)	1 (3)
Respiratory tract infection	7 (22)	0
Dizziness	7 (22)	0
Headache	7 (22)	0
HEMATOLOGICAL AEs ≥10% (N=32)		
Anemia	9 (28)	3 (9)
Thrombocytopenia	9 (28)	2 (6)
Neutropenia	4 (13)	4 (13)

Most adverse events were CTCAE grade 1 or 2

≥ Grade 3 treatment-related AE in 16 (50%) patients
No deaths on study

30 of 32 patients remain on treatment (Median 9 months [range: 4–19])

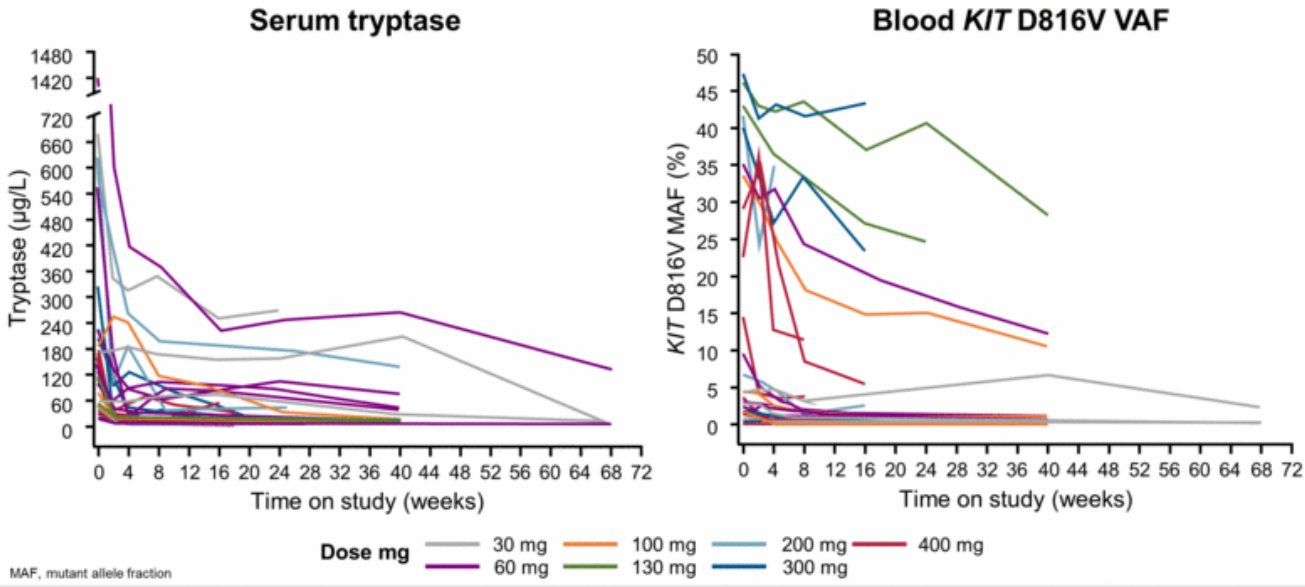
1 discontinued due to PD (AML)

1 investigator decision (wild type *KIT*)

None discontinued due to BLU-285-related AE

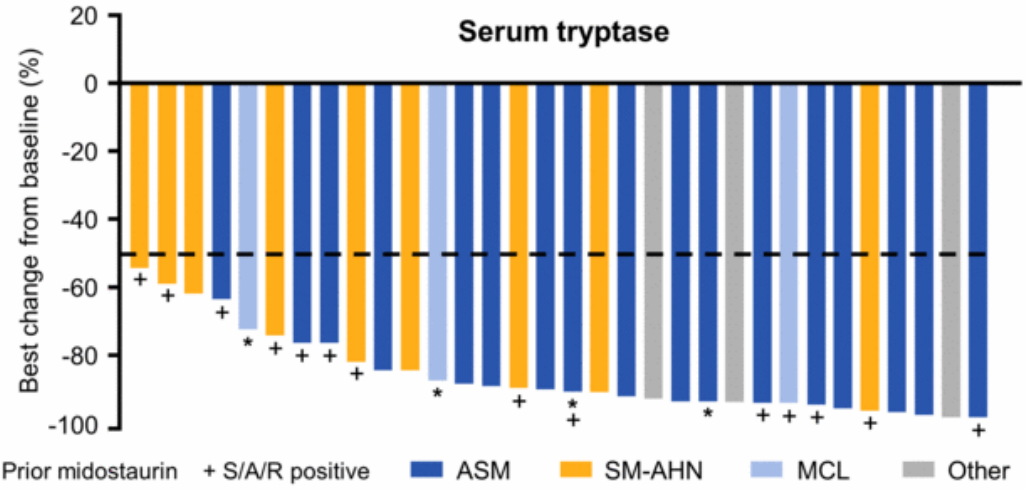
AE, adverse event; AML, acute myeloid leukemia; CTCAE, Common Terminology Criteria for Adverse Events; PD, progressive disease

Rapid and durable decline in tryptase and *KIT* D816V variant allele fraction across all dose levels



MAF, mutant allele fraction

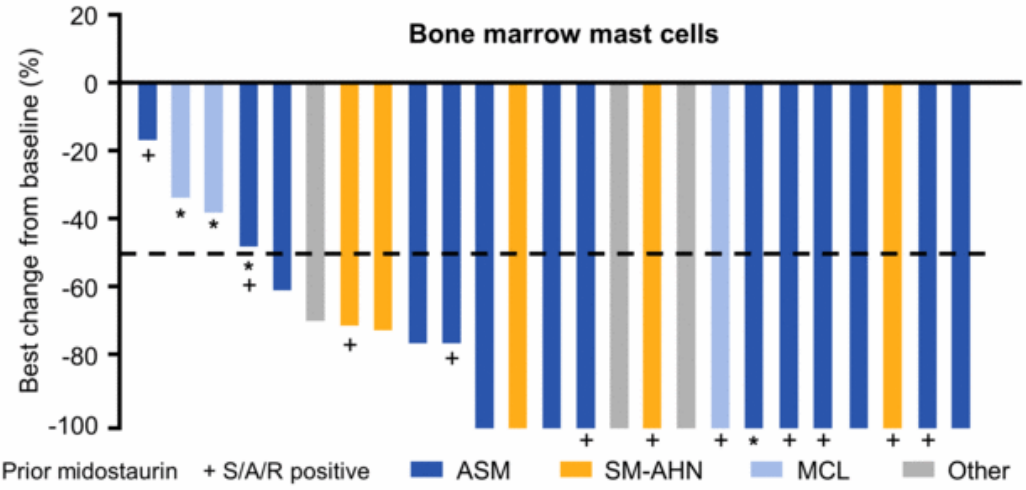
Tryptase decrease in all patients



- Baseline median 124 µg/L, range 14 to 1414 µg/L
- All 32 patients achieved >50% reduction from baseline

Other, SSM (n=2); telangiectasia macularis eruptive perstans (n=1)

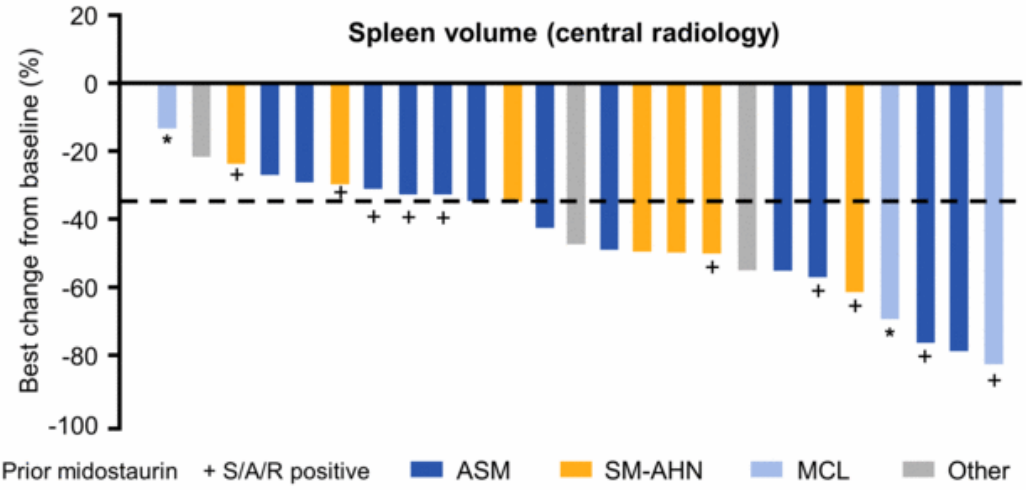
Bone marrow mast cell decrease in all patients^



- Baseline median 20%, range 1.5 to 95%
- ^n=25 evaluable patients with baseline bone marrow mast cells ≥ 5%
- 15/25 (60%) patients achieved bone marrow CR

Other, SSM (n=2); telangiectasia macularis eruptive perstans (n=1)

Spleen volume decrease in all patients^

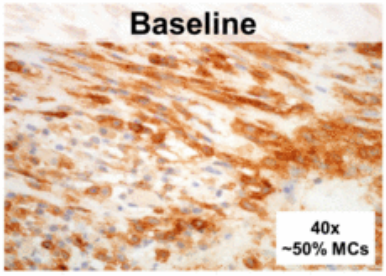


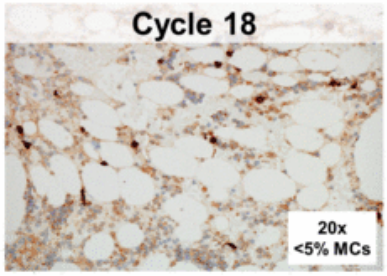
- Baseline median 633 mL, range 130 to 1952 mL
- ^n=25 patients with splenomegaly as per central assessment
- 15/25 (60%) patients achieved >35% reduction of spleen volume

Other, SSM (n=2); telangiectasia macularis eruptive perstans (n=1)

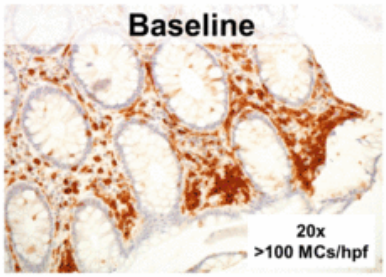
45-year-old female with ASM

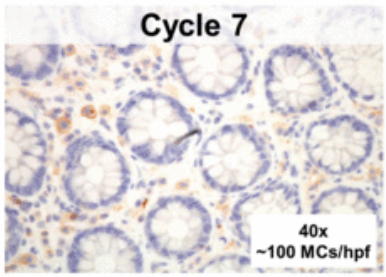
Bone marrow tryptase





Colon CD25



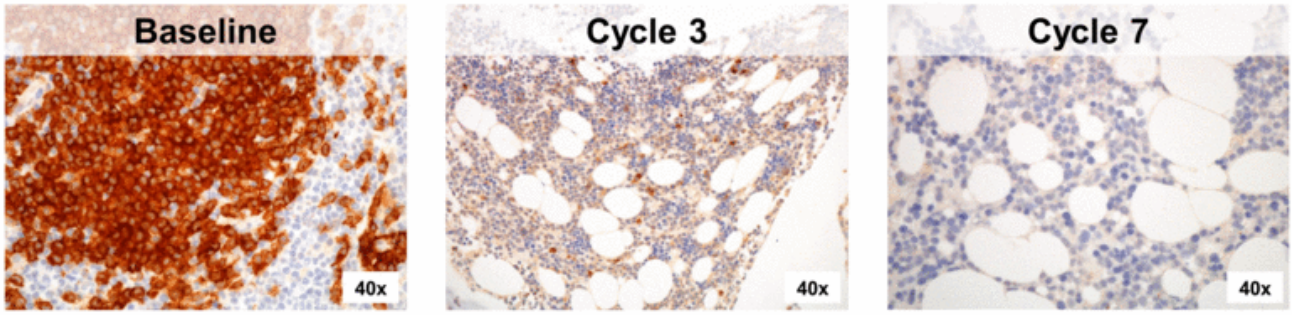


*BLU-285 60 mg; remains on treatment at cycle 18 with confirmed PR per IWG-MRT-ECNM

Images courtesy of Dr Deepti Radia, Guy's and St. Thomas NHS Trust

64-year-old male with MCL

Progressive clearance of bone marrow mast cells



Bone marrow CD117

*BLU-285 200 mg; remains on treatment at cycle 9 with confirmed PR per IWG-MRT-ECNM

Images courtesy of Dr Deepti Radia, Guy's and St. Thomas NHS Trust

Response analysis per IWG-MRT-ECNM criteria

Complete response (CR)[1]

- No bone marrow mast cell aggregate
- Serum tryptase <20 ng/mL
- Peripheral blood count remission
- Complete resolution of C-findings

Partial response (PR)[1]

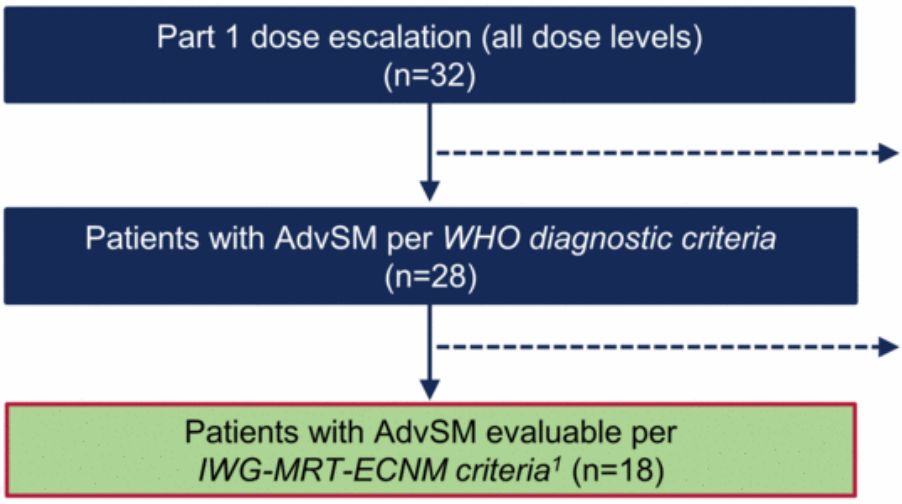
- ≥50% reduction in bone marrow mast cell aggregate
- ≥50% reduction in serum tryptase
- Resolution of 1 or more C-findings

Clinical improvement (CI)[1]

- 1 or more response criteria in absence of CR, PR or PD

[1]Gotlib, et al. Blood. 2013 Mar 28; 121(13): 2393–2401

IWG-MRT-ECNM evaluable patients



Patients invaluable (n=4)

- n=3 non-SM myeloid malignancy
- n=1 *KIT* WT; discontinued prior to post baseline response assessment

Patients excluded (n=10)

- n=6 only had osteolytic bone disease at baseline
- n=4 not measurable per IWG-MRT-ECNM criteria at baseline

WT, wild type; 1. Gotlib J et al Blood (2013) 121:2393

Best overall response per IWG-MRT-ECNM criteria[1]

Best response* n (%) (confirmed and unconfirmed)	ASM (n=7)	SM-AHN# (n=8)	MCL (n=3)	Overall (n=18)
Overall response rate (CR + PR + CI)	6 (86)	5 (63)	2 (67)	13 (72)
CR + PR	5 (71)	4 (50)	1 (33)	10 (56)
Complete response (CR)	2 (29)	0	0	2 (11)
Partial response (PR)	3 (43)	4 (50)	1 (33)	8 (44)
Clinical improvement (CI)	1 (14)	1 (13)	1 (33)	3 (17)
Stable disease (SD)	1 (14)	3 (38)	1 (33)	5 (28)
Progressive disease (PD)	0	0	0	0

- 17 of 18 patients remain on treatment with median duration 9 months (range: 4–19)

*Pending confirmation: ASM, 2 CR; SM-AHN, 3 PR; #Mastocytosis response; 1. Gotlib J et al Blood (2013) 121:2393

BLU-285 has potent, clinically important activity in AdvSM

- Data validate *KIT* D816V as a key disease driver
- Selective targeting of *KIT* D816V with BLU-285 is well tolerated
  - 30 of 32 patients remain on treatment with median duration of 9 months (range: 4–19)
  - RP2D is 300 mg once daily, and expansion is ongoing
- BLU-285 demonstrates high preliminary response rates and durable activity
  - 72% ORR (CR + PR + CI) with 56% CR + PR per IWG-MRT-ECNM criteria
- Additional clinical development with BLU-285, now avapritinib, across the spectrum of systemic mastocytosis is planned for 2018
  - Phase 2 trial in AdvSM
  - Dose finding and Phase 2 trial in ISM and SSM

Acknowledgments

- We thank the participating patients, their families, all study co-investigators, and research coordinators at the following institutions:
  - Deepti Radia, Guy's & St Thomas NHS Trust
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  - Elizabeth Hexner, Abramson Cancer Center at the University of Pennsylvania
  - Albert Quiery, University of Michigan Comprehensive Cancer Center
  - Dan DeAngelo, Dana-Farber Cancer Institute
  - Michael Deininger, University of Utah, Huntsman Cancer Institute
  - Srdan Verstovsek, MD Anderson Cancer Center
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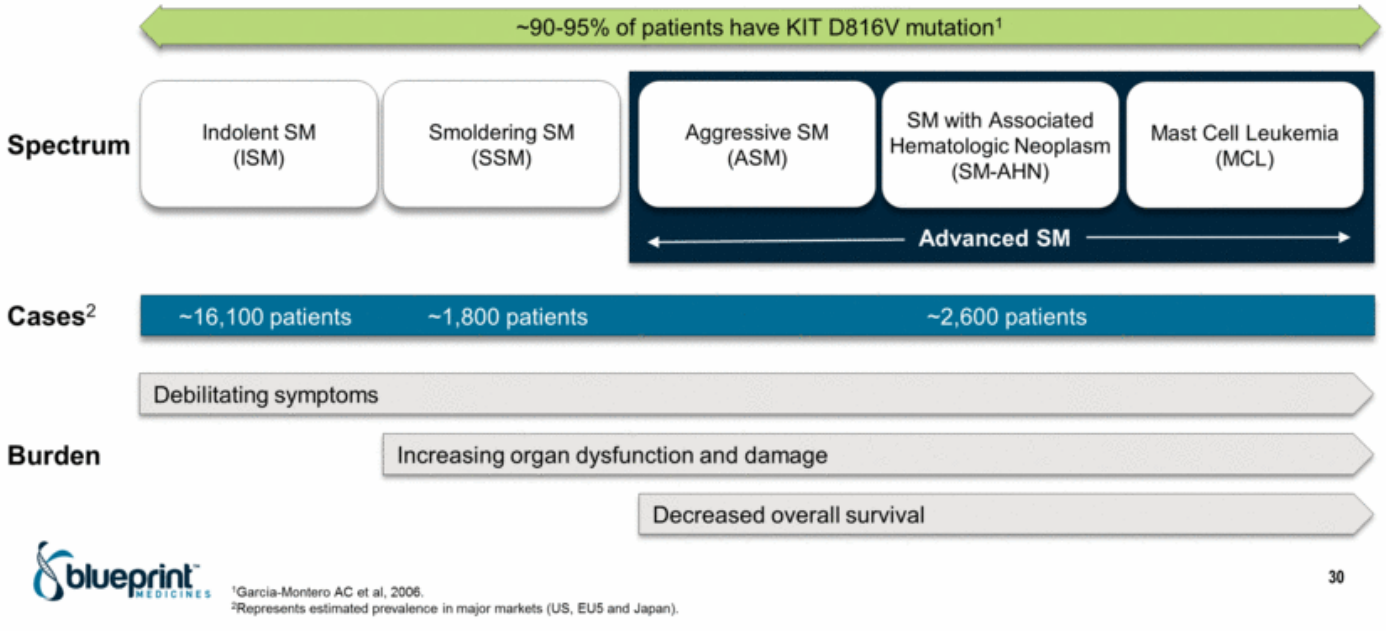
Avapritinib Vision & Next Steps

Andy Boral, MD, PhD
Chief Medical Officer, Blueprint Medicines

Potent and highly selective inhibition of D816V mutant KIT with avapritinib has broad potential applications across the spectrum of SM



[1]Garcia-Montero AC et al, 2006.
[2]Represents estimated prevalence in major markets (US, EU5 and Japan).

Rigorous IWG response criteria for advanced SM have US and EU regulatory precedent

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- No bone marrow mast cell aggregate
- Serum tryptase <20 ng/mL
- Peripheral blood count remission
- Complete resolution of CI-findings

Partial response (PR)[1]

- ≥50% reduction in bone marrow mast cell aggregate
- ≥50% reduction in serum tryptase
- Resolution of 1 or more CI-findings

Clinical improvement (CI)[1]

- 1 or more response criteria in absence of CR, PR or PD

Avapritinib
CR + PR + CI: **72%**
CR + PR: **56%**

Midostaurin
CR + PR + CI: **28%**[2]
CR + PR: **17%**[3]

PD, progressive disease. Data previously presented in December 2017 at the ASH Annual Meeting. Data cutoff: October 4, 2017.
[1]Simplified summary of detailed published criteria (Gotlib, et al. Blood. 2013 Mar 28; 121(13): 2393–2401).
[2]Midostaurin clinical data per IWG-MRT-ECNM criteria from EMA summary of product characteristics.
[3]Midostaurin clinical data per IWG-MRT-ECNM criteria from FDA summary of product characteristics.

A strong foundation for development of avapritinib in SM

Program Status

- ✓ *Favorable tolerability profile*
- ✓ *Strong clinical activity*
- ✓ *Input from SM experts on clinical strategies*
- ● *Feedback from global regulatory authorities*
- ● *Registration-enabling clinical trials*

Key Next Steps

- Plan to engage global regulatory authorities on registration pathways in 1H 2018
- Pending regulatory feedback, plan to initiate:
  - Registration-enabling trial in patients with advanced SM in 1H 2018
  - Dose escalation and proof-of-concept trial in patients with indolent and smoldering SM in 2H 2018
- Continue enrollment of Phase 1 trial throughout 2018

blueprint MEDICINES

Data previously presented in December 2017 at the ASH Annual Meeting. Data cutoff: October 4, 2017.

Questions & Answers