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): **June 15, 2018**

Blueprint Medicines Corporation

(Exact name of registrant as specified in its charter)

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

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

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

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

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

- 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 June 15, 2018, Blueprint Medicines Corporation (the "Company") issued a press release announcing new data from its ongoing Phase 1 clinical trial evaluating avapritinib for the treatment of advanced systemic mastocytosis. The data will be presented on Friday, June 15, 2018 in a poster presentation at the 23rd Congress of the European Hematology Association in Stockholm, Sweden. 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 poster presentation is furnished as Exhibit 99.2 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 and 99.2, 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 June 15, 2018
99.2	Poster presentation by Blueprint Medicines Corporation on June 15, 2018 at the Congress of the European Hematology Association

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: June 15, 2018

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

Blueprint Medicines Announces Updated Data from Ongoing Phase 1 EXPLORER Clinical Trial of Avapritinib in Patients with Advanced Systemic Mastocytosis Showing Profound and Durable Clinical Activity

– Overall Response Rate of 83% –
– Durable Ongoing Responses Up to 22 Months –
– All Patients Evaluable on Measures of Mast Cell Burden Showed Marked Improvements, with 58% Showing Complete Resolution of Bone Marrow Mast Cells –

CAMBRIDGE, Mass., June 15, 2018 – Blueprint Medicines Corporation (NASDAQ:BPMC), a leader in discovering and developing targeted kinase medicines for patients with genomically defined diseases, today announced updated data from its ongoing Phase 1 EXPLORER clinical trial of avapritinib, a potent and highly selective KIT and PDGFRA inhibitor in development for patients with systemic mastocytosis (SM). The updated results confirm and improve upon data previously presented for avapritinib in patients with advanced SM, demonstrating profound and durable clinical activity and favorable tolerability. Advanced SM is a proliferative mast cell disorder associated with severe constitutional symptoms, progressive organ damage and reduced survival.

The updated data from the EXPLORER clinical trial showed an overall response rate (ORR) of 83 percent, as of the data cutoff date of April 30, 2018. Responses were durable and continuing, with a duration of response observed up to 22 months. Seventy-nine percent of responders remained on treatment as of the data cutoff date. All evaluable patients showed marked decreases on one or more objective measures of mast cell burden regardless of advanced SM subtype, previous treatment or dose level. The data will be presented today in a poster presentation at the 23rd Congress of the European Hematology Association (EHA) in Stockholm, Sweden.

Based on the compelling clinical data from the EXPLORER trial and feedback from regulatory authorities, Blueprint Medicines plans to rapidly advance development of avapritinib in a broad population of patients with SM. The Company plans to initiate PATHFINDER, an open-label, single-arm Phase 2 clinical trial in patients with advanced SM, by the middle of 2018. In addition, the Company plans to initiate PIONEER, a randomized, placebo-controlled Phase 2 clinical trial in patients with indolent and smoldering SM, by the end of 2018. Blueprint Medicines believes these clinical trials may support registration of avapritinib in their respective SM patient populations, based on feedback from the U.S. Food and Drug Administration (FDA).

“As a clinician treating patients with this devastating and sometimes fatal rare disease, I’m excited to see that most patients with advanced systemic mastocytosis respond to treatment with avapritinib, and these responses deepen over time and are durable,” said Michael W. Deininger, M.D., Ph.D., Professor and Chief of Hematology and Hematologic Malignancies, Huntsman Cancer Institute at the University of Utah, and an investigator on the Phase 1 trial. “These data further support avapritinib’s unique approach of selectively targeting D816V mutant KIT, the disease driver in most patients with systemic mastocytosis. If these results are confirmed in the planned Phase 2 trial, avapritinib has the potential to become a new standard of care for patients with advanced forms of the disease.”

“These highly encouraging data, coupled with favorable FDA feedback on potential registration pathways, reinforce our commitment to quickly advance the development of avapritinib as a potential treatment for a broad population of patients with systemic mastocytosis,” said Andy Boral, M.D., Ph.D., Chief Medical Officer at Blueprint Medicines. “We look forward to initiating the PATHFINDER trial in patients with advanced systemic mastocytosis by mid-year and expanding our development program with the PIONEER trial in patients with indolent and smoldering forms of the disease by the end of 2018.”

Data from the Ongoing Phase 1 Clinical Trial

As of the data cutoff date of April 30, 2018, 52 patients had been treated with avapritinib in the dose escalation and expansion portions of the Phase 1 EXPLORER clinical trial, including 25 patients with aggressive SM (ASM), 15 patients with advanced SM with an associated hematologic neoplasm (SM-AHN), five patients with mast cell leukemia (MCL), five patients pending central pathology diagnosis, and two patients with smoldering SM. Overall, 35 patients (67 percent) were previously treated, including 10 patients (19 percent) who previously received midostaurin. Patients in the expansion portion of the trial were treated at 300 mg once daily.

Safety Data:

As of the data cutoff date, avapritinib was generally well-tolerated. Most adverse events (AEs) reported by investigators were Grade 1 or 2. Across all grades, the most common treatment-emergent AEs reported by investigators (≥20 percent) included periorbital edema, anemia, fatigue, nausea, diarrhea, peripheral edema, thrombocytopenia, cognitive effects, vomiting, hair color changes and dizziness. Investigators reported treatment-related Grade ≥3 AEs in 28 patients (54 percent).

Among all 52 enrolled patients, 42 remained on treatment as of the data cutoff date. Four patients discontinued treatment with avapritinib due to AEs (three treatment-related and one unrelated). Three patients discontinued treatment with avapritinib due to clinical progression as determined by the investigator. No patients had documented disease progression by IWG-MRT-ECNM criteria. An additional three patients discontinued treatment, including two patients due to an investigator's decision and one patient who withdrew consent.

Clinical Activity Data:

IWG-MRT-ECNM Response Assessment

As of the data cutoff date, 23 patients were evaluable for response by the IWG-MRT-ECNM criteria, a rigorous method of assessing clinical response in patients with advanced SM with regulatory precedent in the U.S. and Europe. Responses were centrally reviewed by a committee of systemic mastocytosis experts.

Across all 23 evaluable patients, the data showed an ORR of 83 percent. Four patients (17 percent) had a confirmed complete response with a full or partial recovery of peripheral blood counts. Twelve patients (52 percent) had a partial response (7 confirmed, 5 pending confirmation) and three patients (13 percent) had clinical improvement (2 confirmed, 1 pending confirmation). The duration of response was up to 22 months, with 79 percent of responders on treatment as of the data cutoff date. All responses observed in the dose escalation portion of the trial have been confirmed, and all responses in the dose expansion portion of the trial are pending confirmation.

Additional Clinical Assessments

All patients evaluable on objective measures of mast cell burden showed clinically significant improvements, regardless of advanced SM subtype, previous treatment or dose level:

- 92 percent of patients had a ≥50 percent decrease in bone marrow mast cells. Among these patients, 58 percent had a complete response (no neoplastic mast cells in bone marrow).
- 98 percent of patients had a ≥50 percent decrease in serum tryptase. Among these patients, 66 percent had a complete response (serum tryptase level <20 µg/L).
- 95 percent of patients had a ≥35 percent decrease in spleen volume or a ≥50 percent decrease by palpation. Among these patients, 47 percent had a complete response (normal spleen length).
- 88 percent of patients had ≥50 percent decrease in KIT D816V mutant allele burden.

In addition, 87 percent of patients had improvement in skin symptoms, based on investigator assessments.

Clinical Activity in Patients with Smoldering SM

Two patients with smoldering SM, an intermediate form of SM, were treated with avapritinib in the EXPLORER clinical trial. Consistent with the broader trial population, the patients with smoldering SM showed clinically significant improvements on multiple measures of mast cell burden. Among these two patients with smoldering SM, one patient had a bone marrow mast cell complete response, and both patients had a serum tryptase complete response. Blueprint Medicines believes these results, together with data from the EXPLORER trial showing clinical activity across all doses tested, support further development of avapritinib as a potential treatment for patients with indolent and smoldering SM.

About the Phase 1 EXPLORER Clinical Trial for Avapritinib in Advanced SM

The Phase 1 EXPLORER clinical trial of avapritinib is designed to evaluate the safety and tolerability of avapritinib in adults with advanced SM. The trial is currently 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 EXPLORER 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. To learn more about the EXPLORER trial, visit www.clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT02561988).

Patients and physicians interested in the Phase 1 EXPLORER or Phase 2 PATHFINDER trials for avapritinib in advanced SM or the Phase 2 PIONEER trial for avapritinib in indolent and smoldering SM can contact the Blueprint Medicines study director at studydirector@blueprintmedicines.com or 1-617-714-6707.

About SM

In approximately 90 to 95 percent of all SM cases, constitutively active KIT D816V protein is present and is central to disease pathogenesis. *KIT* activation leads to increased degranulation, proliferation, and survival of mast cells, which in turn leads to constitutional symptoms such as pruritus, flushing, headaches, bone pain, nausea, vomiting, and diarrhea. In advanced cases of SM, mast cell infiltration leads to organ damage and reduced survival. There are several forms of SM, including indolent SM, smoldering SM and more advanced forms of SM, which include ASM, SM-AHN and MCL. Patients with advanced SM have a poor prognosis, with a median overall survival of approximately 3.5 years in patients with ASM, 2 years in those with SM-AHN, and less than 6 months in those with MCL. Currently, there are no approved therapies for advanced SM that selectively target the KIT D816V mutation. Patients with indolent SM suffer from a broad range of moderate to severe acute and chronic symptoms that are poorly controlled by symptom-directed therapies and have significant impact on quality of life. Currently, there are no approved treatments for patients with indolent SM.

About Avapritinib

Avapritinib is an orally available, potent and highly selective inhibitor of KIT and PDGFRA. In certain diseases, a spectrum of clinically relevant mutations forces the KIT or PDGFRA protein kinases into an increasingly active state. Avapritinib is uniquely designed to bind and inhibit the active conformation of these proteins, including KIT D816V and PDGFRα D842V at sub-nanomolar potency. Blueprint Medicines is initially developing avapritinib, an investigational medicine, for the treatment of patients with advanced gastrointestinal stromal tumors (GIST) and systemic mastocytosis.

In June 2017, avapritinib received Breakthrough Therapy Designation from the FDA for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRα D842V mutation. Previously, the FDA granted orphan drug designation to avapritinib for mastocytosis and GIST and fast track designation to avapritinib for GIST. In addition, the European Commission has granted orphan drug designation to avapritinib for GIST. In May 2018, Blueprint Medicines announced plans to submit a New Drug Application to the FDA for avapritinib for the treatment of PDGFRα D842V-

driven GIST in the first half of 2019. In June 2018, Blueprint Medicines announced an exclusive collaboration and license agreement with CStone Pharmaceuticals for the development and commercialization of avapritinib and certain other drug candidates in Mainland China, Hong Kong, Macau and Taiwan.

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 disease driven by the abnormal activation of kinases. Blueprint Medicines is advancing multiple 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 Notes 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, including plans and timelines for initiating the Phase 2 PATHFINDER clinical trial of avapritinib in patients with advanced SM and plans and timelines for initiating the Phase 2 PIONEER clinical trial of avapritinib in patients with indolent and smoldering SM; expectations regarding the potential for the Phase 2 PATHFINDER clinical trial and for the Phase 2 PIONEER clinical trial to be registration-enabling for avapritinib in their respective patient populations; Blueprint Medicines' ability to implement its clinical development plans for avapritinib in SM; expectations regarding the potential benefits of avapritinib in treating patients with SM, including avapritinib's potential to become a new standard of care for patients with advanced SM; expectations regarding the development of avapritinib as a treatment for patients with indolent SM and smoldering 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 candidates, including avapritinib, BLU-554, BLU-667 and BLU-782; 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; 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 hepatocellular carcinoma, avapritinib for PDGFRα D842V-driven GIST and BLU-667 for RET-driven non-small cell lung cancer; the success of Blueprint Medicines' current and future collaborations, including its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. and its collaboration with CStone Pharmaceuticals. 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 March 31, 2018, as filed with the Securities and Exchange Commission (SEC) on May 2, 2018, and any other filings that Blueprint Medicines has made or may make with the SEC in the future. Any forward-looking statements contained in this press release represent Blueprint Medicines' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Blueprint Medicines explicitly disclaims any obligation to update any forward-looking statements.

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Avapritinib (BLU-285), a Selective KIT Inhibitor, is Associated with High Response Rate and Tolerable Safety Profile in Advanced Systemic Mastocytosis: Results of a Phase 1 Study

Michael W. Deininger[1], Jason Gotlib[2], William A. Robinson[3], Deepti H. Radia[4], Mark W. Drummond[5], Albert T. Quiery[6], Elizabeth Hexner[7], Srdan Verstovsek[8], Hongliang Shi[9], Oleg Schmidt-Kittler[9], Meera Tugnait[9], Maureen G. Conlan[9], Daniel J. DeAngelo[10].
[1]University of Utah, Salt Lake City, USA; [2]Stanford Cancer Institute/Stanford University School of Medicine, Stanford, USA; [3]University of Colorado Denver, Aurora, USA; [4]Guys and St Thomas NHS Foundation, London, UK; [5]Beatson Cancer Centre, Glasgow, UK; [6]University of Michigan, Ann Arbor, USA; [7]University of Pennsylvania, Philadelphia, USA; [8]University of Texas MD Anderson Cancer Center, Houston, USA; [9]Blueprint Medicines Corporation, Cambridge, USA; [10]Dana-Farber Cancer Institute, Boston, Massachusetts, USA.

Background

- Systemic mastocytosis (SM) encompasses a spectrum of mast cell disorders characterized by an accumulation of neoplastic mast cells in tissues/visceral organs[1,2]
- Constitutively active mutant KIT (typically D816V) is present in 90–95% of SM cases and is central to disease pathogenesis[3-5]
- Advanced systemic mastocytosis (AdvSM) is the most severe form of SM comprising three subtypes, aggressive SM (ASM), SM with an associated hematologic neoplasm (SM-AHN), and mast cell leukemia (MCL),[1,2] classified using the World Health Organization (WHO) diagnostic criteria[5,6]
- The multi-kinase inhibitor midostaurin is currently the only approved treatment for all subtypes of AdvSM, but is not optimized for selective KIT D816V inhibition[7,8]
- Avapritinib is a highly potent and selective kinase inhibitor, developed to specifically target the active conformation of KIT, conferring potent and selective inhibition of KIT D816V and other activation loop mutants[9]

Methods

Study design and assessments

- EXPLORER is a two-part, Phase 1, multicenter study of avapritinib in adult patients with AdvSM or relapsed/refractory myeloid malignancies (Figure 1, Table 1)

Figure 1. Study design

- **Primary objectives:** MTD/RP2D and safety profile
- **Secondary objectives:** Preliminary antineoplastic activity and PK

ASM, aggressive systemic mastocytosis; MCL, mast cell leukemia; MTD, maximum tolerated dose; QD, once daily; RP2D, recommended Phase 2 dose; SM-AHN, systemic mastocytosis with associated hematologic neoplasm
*As of 30 April 2018, 20 patients have been enrolled in Part 2

- **Antineoplastic activity was assessed by:** Changes in percentage of bone marrow mast cells, splenomegaly, serum tryptase, KIT D816V mutant allele burden
  - Overall response assessed by modified International Working Group Myeloproliferative Neoplasms Research and Treatment and European Competence Network on Mastocytosis criteria (m-IWG-MRT-ECNM)
    - C-findings per m-IWG-MRT-ECNM criteria necessary for response assessment
    - Complete response (CR) with partial recovery of peripheral blood counts (CRh) added to accommodate CR with residual cytopenias due to avapritinib
    - Response is confirmed 12 weeks after first documentation of response
    - Response adjudicated by a Response Adjudication Committee (RAC), composed of subset of study investigators

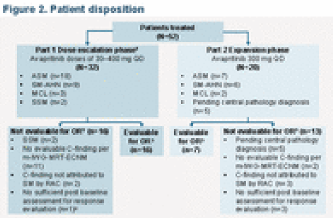
Table 1. Patient population

Key inclusion criteria	Key exclusion criteria
Diagnosis of AdvSM (ASM, SM-AHN or MCL) per WHO criteria or a relapsed/refractory myeloid malignancy	Diagnosis of acute myeloid leukemia
≥1 "C-finding" based on WHO criteria for diagnosis of ASM and SM-AHN	High-risk myelodysplastic syndrome or Philadelphia chromosome positive malignancy
Age ≥18 years	Brain metastases or risk for CNS hemorrhage
ECOG performance score (PS) of 0–3	

Results

- As of 30 April 2018, a total of 52 patients received avapritinib; 32 in Part 1 and 20 in Part 2 (Figure 2)
- Median duration of treatment was 14 months (range 1-26 months) in Part 1 and 5 months (range 1-9 months) in Part 2; 42 (80%) patients remain on treatment
- Baseline demographics and disease characteristics for all 52 patients are shown in Table 2

Figure 2. Patient disposition


Patients treated (N=52)
Part 1 Dose escalation phase*
Avapritinib doses of 30–400 mg QD
(N=32)
ASM (n=18)
SM-AHN (n=9)
MCL (n=3)
SSM (n=2)
Part 2 Expansion phase
Avapritinib 300 mg QD
(N=20)
ASM (n=7)
SM-AHN (n=6)
MCL (n=2)
Pending central pathology diagnosis (n=5)
Not evaluable for OR† (n=16)
SSM (n=2)
No evaluable C-finding per m-IWG-MRT-ECNM (n=11)
C-finding not attributed to SM by RAC (n=2)
No sufficient post baseline assessment for response evaluation (n=1)‡
Evaluable for OR† (n=16)
Evaluable for OR† (n=7)
Not evaluable for OR† (n=13)
Pending central pathology diagnosis (n=5)
No evaluable C-finding per m-IWG-MRT-ECNM (n=2)
C-finding not attributed to SM by RAC (n=3)
No sufficient post baseline assessment for response evaluation (n=3)

OR, overall response; RAC, Response Adjudication Committee; SSM, smoldering systemic mastocytosis; WT, wild-type.
* Additional accrual was allowed in dose levels declared safe † Based on m-IWG-MRT-ECNM criteria.
‡ KIT wild-type, discontinued prior to post baseline response assessment

Table 2. Patient demographics and disease characteristics

Characteristic, n (%)	Part 1 (N=32)	Part 2 (N=20)	All patients (N=52)
Age (years), median (range)	63 (34, 83)	62 (40, 77)	63 (34, 83)
Gender, male	16 (50)	11 (55)	27 (52)
Prior cytoreductive therapy	20 (69)	13 (65)	35 (67)
Number of prior cytoreductive therapies			
0	10 (31)	7 (35)	17 (33)
1	13 (41)	9 (45)	22 (42)
2	7 (22)	2 (10)	9 (17)
3	2 (6)	2 (10)	4 (8)
ECOG PS			
0	7 (22)	6 (30)	13 (25)
1–2	25 (78)	10 (50)	35 (67)
3	0	4 (20)	4 (8)
KIT Exon 17 mutation status[a]			
D816V	28 (88)	17 (85)	45 (87)
D816Y	1 (3)	0	1 (2)
Wild-type	3 (9)	3 (15)	6 (12)
Bone marrow MC burden (% MC)[b], median (range)	20 (1.5, 95.0)	50 (10.0, 95.0)	25 (1.5, 95.0)
Serum tryptase (µg/L), median (range)	124 (14, 1414)	216 (13, 491)	161 (13, 1414)
Spleen volume (mL)[c], median (range)	626 (130, 1952)	1064 (359, 1923)	695 (130, 1952)
KIT D816V mutant allele burden (%)[d], median (range)	4.40 (0.09, 47.30)	23.45 (0.16, 80.10)	11.52 (0.09, 80.10)
Mastocytosis in the skin	14 (44)	9 (45)	23 (44)

ECOG PS, Eastern Cooperative Oncology Group performance score; MC, mast cell. a Based on local testing.
b Results for Part 1 patients are based on local assessment; results for Part 2 patients are based on central pathology review (N=8).
c Spleen volume assessed by Central Radiology Review (N=46). d Mutation allele burden (%) assessed by Central Laboratory (Molecular MD) using a validated ddPCR assay with limit of detection of 0.17% mutant allele fraction (N=50).

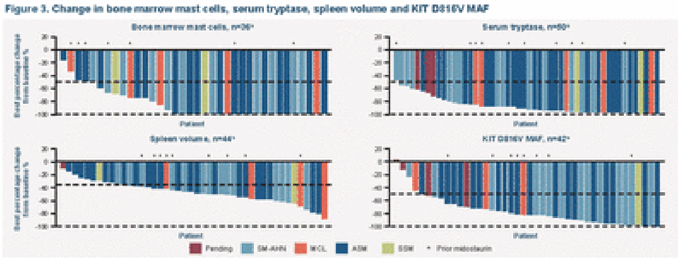
Antineoplastic activity

Table 3. Antineoplastic activity: changes in measures of mast cell burden

Best Response, n (%)	Part 1 (N=32)	Part 2 (N=20)	All patients (N=52)
Bone marrow MCs	**27***	**9**	**36**
No neoplastic MCs present	16 (59)	5 (56)	21 (58)
≥50% decrease in neoplastic MCs[a]	8 (30)	4 (44)	12 (33)
<50% decrease in neoplastic MCs	3 (11)	0	3 (8)
Serum tryptase[b]	**32***	**18**	**50**
<20 µg/L	24 (75)	9 (50)	33 (66)
≥50% decrease	8 (25)	8 (44)	16 (32)
<50% decrease	0	1 (6)	1 (2)
Splenomegaly[c]	**11**	**8**	**19**
Normal spleen length by imaging or nonpalpable	6 (55)	3 (38)	9 (47)
≥35% decrease in spleen volume by imaging or ≥50% reduction by palpation	5 (45)	4 (50)	9 (47)
<35% decrease in spleen size by imaging or <50% reduction by palpation	0	1 (13)	1 (5)
KIT D816V mutant allele burden in bone marrow[d]	**26**	**16**	**42**
≥50% decrease	23 (88)	14 (88)	37 (88)
<50% decrease	3 (12)	1 (6)	4 (10)
Increase	0	1 (6)	1 (2)
Mastocytosis in the skin	**14**	**9**	**23**
Improvement based on investigator assessment	13 (93)	7 (78)	20 (87)

MC, mast cells. Footnotes: [illegible]

Figure 3. Change in bone marrow mast cells, serum tryptase, spleen volume and KIT D816V MAF



MAF, mutant allele fraction; *number of patients evaluable for each parameter

Table 4. Best overall response per m-IWG-MRT-ECNM criteria

Response, n (%)	Part 1 (Best confirmed response) ASM (n=7)	Part 1 SM-AHN (n=6)	Part 1 MCL (n=3)	Part 1 All (n=16)	Part 2 (Best unconfirmed response)* ASM (n=1)	Part 2 SM-AHN (n=4)	Part 2 MCL (n=2)	Part 2 All (n=7)	Part 1 and 2 All (n=23)
ORR (CR/CRh + PR + CI)	6 (86)	4 (67)	3 (100)	**13 (81)**	1 (100)	3 (75)	2 (100)	**6 (86)**	**19 (83)**
Clinical Benefit Rate (CR/CRh + PR + CI + SD)	7 (100)	6 (100)	3 (100)	**16 (100)**	1 (100)	4 (100)	2 (100)	**7 (100)**	**23 (100)**
CR/CRh + PR	5 (71)	4 (67)	2 (67)	**11 (69)**	1 (100)	2 (50)	2 (100)	**5 (71)**	**16 (70)**
CR/CRh	4 (57)	0	0	**4 (25)**	0	0	0	**0**	**4 (17)**
CR	1 (14)	0	0	**1 (6)**	0	0	0	**0**	**1 (4)**
CRh	3 (43)	0	0	**3 (19)**	0	0	0	**0**	**3 (13)**
PD	0	0	0	**0**	0	0	0	**0**	**0**

ORR, overall response rate; CI, clinical improvement; PR, partial response; SD, stable disease; clinical improvement; PD, progressive disease; *pending 12 week confirmation

Overall response rate per modified IWG-MRT-ECNM criteria

- In Part 1 and Part 2 of the study, 16 and 7 patients, respectively, were evaluable for response per m-IWG-MRT-ECNM criteria. Response data are presented in Table 4
- In Part 1, all responses were confirmed at 12 weeks
  - Time to response was rapid, with most patients (11/13, 85%) experiencing first evidence of response at the start of Cycle 3; median time to first resolution of at least one evaluable C-finding was 36 days
  - Duration of response ranged from 8 to 22 months
- In Part 2, all responses were unconfirmed (pending 12 week confirmation)
- 15/19 (79%) responding patients remain on treatment

Reduction in mast cell burden

- In both Part 1 and Part 2, a high rate of response was observed for each measure of mast cell burden (Figure 3, Table 3); this was consistent across all subtypes of AdvSM
- Among 36 patients with bone marrow mast cells ≥5% and post baseline bone marrow assessment and tryptase measurement, 29 (81%) had ≥ 50% reduction in both parameters

Safety

- 50 patients (96%) reported an adverse event (AE) occurring at any grade (Table 5); Grade ≥3 treatment-related AEs were reported in 28 (54%) patients
- Other AEs of interest include: ascites (n=5 [10%], n=2 [4%] at ≥Grade 3) and pleural effusion (n=5 [10%], n=0 at ≥Grade 3)
- Dose reductions and interruptions due to AEs were reported in 29 (56%) patients each, most of which occurred at doses >200 mg QD
- Ten patients discontinued from study treatment: n=4, AE (Grade 4 related refractory ascites, Grade 5 unrelated sepsis, Grade 2 related encephalopathy, Grade 2 related confusional state); n=3 clinical progression (not meeting criteria for PD per m-IWG-MRT-ECNM criteria), n=2, investigator's decision, n=1 withdrawal of consent

Table 5. Adverse events reported in ≥20% of patients (N=52)

AE, n (%)	AEs regardless of study drug relationship: Any grade	Grade 1	Grade 2	Grade ≥3	Any grade treatment-related
Non-hematological					
Periorbital edema	32 (62)	22 (42)	8 (15)	2 (4)	32 (62)
Fatigue	21 (40)	9 (17)	9 (17)	3 (6)	16 (31)
Nausea	19 (37)	10 (19)	7 (13)	2 (4)	17 (33)
Diarrhea	18 (35)	10 (19)	6 (12)	1 (2)	13 (25)
Peripheral edema	18 (35)	14 (27)	3 (6)	0	14 (27)
Cognitive effects[a]	13 (25)	8 (15)	4 (8)	1 (2)	10 (19)
Vomiting	13 (25)	7 (13)	3 (6)	3 (6)	10 (19)
Hair color changes	12 (23)	11 (21)	0	1 (2)	12 (23)
Dizziness	11 (21)	9 (17)	2 (4)	0	6 (12)
Hematological					
Anemia	22 (42)	6 (12)	8 (15)	8 (15)	17 (33)
Thrombocytopenia	16 (31)	5 (10)	2 (4)	9 (17)	10 (19)

a Cognitive effects include the following AE terms: cognitive disorder, confusional state, and memory impairment

Conclusions

- Avapritinib has potent antineoplastic activity across all subtypes of AdvSM, with an ORR of 83% per m-IWG-MRT-ECNM criteria, and responses were durable
- Avapritinib treatment resulted in deep and durable reductions in levels of bone marrow mast cells, serum tryptase, splenomegaly and KIT D816V mutant allele burden, as well as reversal of organ damage, in all subtypes of AdvSM, regardless of prior treatment
- 50% or greater reduction in both BM mast cells and tryptase occurred in 81% of patients, including those not evaluable for response by m-IWG-MRT-ECNM criteria
- Avapritinib was well-tolerated, and the majority of patients remain on study treatment
- Expansion (Part 2) is ongoing and Phase 2 PATHFINDER study is planned to start enrollment by the middle of 2018 to further investigate efficacy and tolerability of avapritinib in AdvSM
- Data support further evaluation of avapritinib across the spectrum of SM, including indolent SM and smoldering SM; a Phase 2 clinical study (PIONEER) is planned to start in these indications by the end of 2018

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EXPLORER Advanced SM