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 2, 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 December 2, 2018, Blueprint Medicines Corporation issued a press release announcing updated data from its ongoing Phase 1 EXPLORER clinical trial evaluating avapritinib for the treatment of advanced systemic mastocytosis. The data were presented on Sunday, December 2, 2018 in an oral presentation at the 60th American Society of Hematology Annual Meeting and Exposition ("ASH Annual Meeting") in San Diego, California. 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.

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 December 2, 2018
99.2	Presentation by Blueprint Medicines Corporation at the ASH Annual Meeting on December 2, 2018

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 3, 2018

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

Blueprint Medicines Announces Updated Results from Ongoing EXPLORER Clinical Trial of Avapritinib Demonstrating Broad Clinical Activity and Significant Symptom Reductions in Patients with Systemic Mastocytosis

- 83% overall response rate, with evidence of deepening of response over time -
- Median duration of response not reached; 12-month duration of response rate of 76% -
- Statistically significant improvements in patient-reported disease symptoms observed -
- 7 of 7 enrolled patients with indolent and smoldering SM showed improvements in mast cell burden and patient-reported disease symptoms -

CAMBRIDGE, Mass, December 2, 2018 – Blueprint Medicines Corporation (NASDAQ: BPMC), a leader in discovering and developing targeted kinase medicines for patients with genomically defined diseases, today announced updated results for the Phase 1 EXPLORER clinical trial of avapritinib, a potent and highly selective inhibitor of D816V mutant KIT, the common disease driver in nearly all patients with systemic mastocytosis (SM). The updated EXPLORER trial data in patients with advanced SM showed durable clinical responses that deepened over time, regardless of disease subtype, prior therapy or starting dose. Avapritinib was generally well-tolerated, and most adverse events (AEs) reported by investigators were Grade 1 or 2. These results will be presented today in an oral presentation at the 60th American Society of Hematology Annual Meeting and Exposition in San Diego, California.

As of the data cutoff date of September 30, 2018, the updated results from the ongoing EXPLORER trial showed an overall response rate (ORR) of 83 percent. Twenty-four percent of patients had a complete response with a full or partial recovery of peripheral blood counts (CR/CRh). Responses deepened over time, with a median time to initial response of two months and a median time to CR/CRh of nine months. The median duration of response (DoR) was not reached, and the 12-month DoR rate was 76 percent.

In addition, statistically significant improvements in patient-reported disease symptoms were observed. A 41 percent mean reduction (p=0.043) in patient-reported disease symptoms was demonstrated on the Advanced SM Symptom Assessment Form (AdvSM-SAF), the first patient-reported outcomes tool designed specifically to assess advanced SM.

“Systemic mastocytosis is a complex rare disorder that causes debilitating symptoms across all forms of the disease and reduced survival in advanced patients,” said Jason Gotlib, M.D., professor of Medicine, Hematology, at the Stanford University Medical Center and an investigator on the EXPLORER trial. “The updated EXPLORER study results show that selectively targeting D816V mutant KIT with avapritinib led to profound and durable clinical activity in patients with advanced systemic mastocytosis, including significant improvements in patient-reported disease symptoms and quality of life. Combined with encouraging preliminary data from an initial cohort of indolent systemic mastocytosis patients from the EXPLORER study, these results highlight the potential of avapritinib to improve objective and subjective measures of disease burden across the spectrum of mastocytosis subtypes.”

“The data further validate Blueprint Medicines’ precision therapy approach, where we target genetic drivers of disease with potent and highly selective inhibitors,” said Andy Boral, M.D., Ph.D., Chief Medical Officer of Blueprint Medicines. “With robust clinical data from the EXPLORER trial, favorable FDA feedback on potential registration pathways and Breakthrough Therapy Designation for advanced systemic mastocytosis, we believe avapritinib has a strong foundation for expedited development across all forms of the disease. In particular, the new data showing a significant decrease in symptom burden in patients enrolled in the EXPLORER trial increase our confidence in avapritinib’s potential in indolent systemic mastocytosis.”

Data Highlights from the Ongoing Phase 1 EXPLORER Clinical Trial

As of the data cutoff date of September 30, 2018, 67 patients were treated with avapritinib in the dose escalation and expansion portions of the Phase 1 EXPLORER clinical trial, including 23 patients with aggressive SM (ASM), 30 patients with advanced SM with an associated hematological neoplasm (SM-AHN), seven patients with mast cell leukemia (MCL) and seven patients with indolent or smoldering SM. Forty patients (60 percent) had a prior treatment, including 14 patients (23 percent) who had previously received Rydapt® (midostaurin).

Safety Data

As of the data cutoff date, avapritinib was generally well-tolerated. Most AEs were reported by investigators as Grade 1 or 2. Across all enrolled patients, 52 patients (78 percent) remained on treatment as of the data cutoff date. Three patients (4 percent) discontinued treatment with avapritinib due to treatment-related AEs.

Across all grades, the most common non-hematological treatment-emergent AEs (regardless of relationship to avapritinib) reported by investigators (>15 percent) were periorbital edema, fatigue, nausea, diarrhea, peripheral edema, vomiting, cognitive effects, hair color changes, arthralgia, dizziness and abdominal pain. The most common hematological treatment-emergent AEs reported by investigators (>10 percent) were anemia, thrombocytopenia and neutropenia. Grade 3 and 4 treatment-related AEs occurred in 44 patients (66 percent), and these events were most commonly hematological AEs, typically in patients with low blood counts (cytopenias) at study entry.

Clinical Activity Data

IWG-MRT-ECNM Assessments and Objective Measures of Mast Cell Burden

As of the data cutoff date, 29 patients were evaluable for response by the modified IWG-MRT-ECNM criteria, a rigorous method for assessing clinical response in advanced SM patients with regulatory precedent in the U.S. and Europe. Responses were centrally reviewed by a committee of SM experts.

Avapritinib demonstrated durable clinical responses across all doses studied and in each subtype of advanced SM – ASM, SM-AHN and MCL. The duration of treatment was up to 31 months as of the data cutoff date, with a median follow-up time of 14 months in evaluable patients.

Across all evaluable patients at all doses, the ORR was 83 percent. Seven patients had a CR/CRh (24 percent, two pending confirmation), 14 patients had a partial response (48 percent, three pending confirmation) and three patients had clinical improvement (10 percent, one pending confirmation). Three of the pending responses were previously confirmed responses (two partial responses, one clinical improvement) that are transitioning to a deeper response. No patients had documented disease progression per modified IWG-MRT-ECNM criteria.

In addition, strong clinical activity was demonstrated in evaluable patients treated with a starting dose of less than or equal to 200 mg once daily (QD), the dose under evaluation in the ongoing registration-enabling Phase 2 PATHFINDER clinical trial in patients with advanced SM. These 10 patients had an ORR of 90 percent and a CR/CRh rate of 50 percent (one complete response pending confirmation).

All patients evaluable on objective measures of mast cell burden showed reductions from baseline. These results were shown regardless of disease subtype, prior therapy (including midostaurin or the investigational agent DCC-2618), or co-mutation status. These measures consisted of declines in bone marrow mast cells, serum tryptase, spleen volume and KIT D816V mutant allele burden.

At baseline, 22 SM patients received steroids for mastocytosis symptoms. As of the data cutoff date, 18 patients (80 percent) decreased their steroid dose, including nine patients (41 percent) who were able to entirely discontinue their steroids.

Patient-Reported Outcomes

As of the data cutoff date, 32 patients in the dose expansion portion of the Phase 1 EXPLORER trial were evaluated using the AdvSM-SAF, the first patient-reported outcomes tool developed specifically for advanced SM patients. It was designed to evaluate symptoms across the gastrointestinal domain (abdominal pain, diarrhea, nausea and vomiting) and skin domain (spots, itching and flushing), as well as fatigue. Patients reported their symptoms daily using an electronic diary.

In advanced SM patients, benefits were shown across each individual symptom studied. There was a 41 percent improvement from baseline in the AdvSM-SAF Total Symptom Score (p=0.043). The most symptomatic patients (n=16, top 50th percentile) had the largest mean improvement in the AdvSM-SAF Total Symptom Score (46 percent, p=0.038).

In addition, an improvement in patient-reported quality of life was observed. As of the data cutoff date, 30 patients were evaluated using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-30), a validated and commonly used patient-reported outcomes tool in oncology clinical trials. Results showed a statistically significant improvement in quality of life score, approaching levels observed in healthy aged-matched controls, with a pronounced improvement observed in the most symptomatic patients.

Proof-of-Concept in Indolent and Smoldering SM

All evaluable patients with indolent and smoldering SM showed profound reductions in bone marrow mast cells, serum tryptase, spleen volume and KIT D816V mutant allele burden. The data also showed avapritinib led to improvements in patient-reported symptoms. These encouraging data support Blueprint Medicines' planned Phase 2 PIONEER clinical trial in patients with indolent and smoldering SM.

About the Clinical Development Program for Avapritinib in SM

Blueprint Medicines is pursuing a broad clinical development program for avapritinib across advanced, indolent and smoldering forms of SM. Avapritinib is currently being evaluated in two ongoing clinical trials for advanced SM: the Phase 1 EXPLORER clinical trial and the registration-enabling Phase 2 PATHFINDER clinical trial.

The Phase 1 EXPLORER clinical trial of avapritinib was designed to identify the recommended Phase 2 dose for further study and demonstrate proof-of-concept in advanced SM. The dose escalation portion is complete, and the expansion portion of the trial is enrolling patients with ASM, SM-AHN and MCL at multiple sites in the United States and United Kingdom. Trial objectives include assessing safety and tolerability, response per modified IWG-MRT-ECNM criteria and patient-reported outcomes.

The Phase 2 PATHFINDER clinical trial is an open-label, single-arm, registration-enabling clinical trial in patients with advanced SM. Patient dosing is now ongoing in the clinical trial, which is designed to enroll up to 60 advanced SM patients at sites in the United States, Canada and Europe. The primary efficacy endpoints are ORR and DoR based on modified IWG-MRT-ECNM criteria.

Blueprint Medicines expects to initiate the Phase 2 PIONEER clinical trial, a randomized, placebo-controlled, registration-enabling trial in patients with indolent and smoldering SM, by the end of 2018. The trial's primary endpoint will be symptom reductions for avapritinib versus placebo based on the Indolent and Smoldering SM Assessment Form Total Symptom Score. All patients who complete the dose-finding (part 1) and placebo-controlled efficacy (part 2) portions of this trial will have an opportunity to receive avapritinib in an open-label extension (part 3).

SM patients and clinicians interested in ongoing or planned clinical trials can contact the Blueprint Medicines study director at SM@blueprintmedicines.com or 1-617-714-6707. Additional details are available at www.pathfindertrial.com, www.pioneertrial.com or www.clinicaltrials.gov.

About SM

SM results from the abnormal proliferation and survival of mast cells, which mediate allergic responses. There are several forms of the disease, including indolent SM, smoldering SM and three advanced subtypes – ASM, SM-AHN and MCL. The KIT D816V mutation drives approximately 90 to 95 percent of all SM cases, causing debilitating and difficult-to-manage symptoms such as pruritus, flushing, headaches, bone pain, nausea, vomiting, diarrhea, anaphylaxis, abdominal pain and fatigue. While these effects occur across SM patients, symptom burden and poor quality of life are the predominant disease manifestations of indolent and smoldering SM. Advanced SM patients experience organ damage and a median overall survival of about 3.5 years in ASM, two years in SM-AHN and less than six months in MCL.

Currently, there are no approved therapies that selectively inhibit KIT D816V in advanced SM, and no approved therapies for indolent and smoldering SM. New treatments are needed that are more effective and better tolerated than existing advanced SM therapy, as well as for indolent and smoldering SM patients whose symptoms are often not well controlled with symptom-directed therapies.

About Avapritinib

Avapritinib is a potent and selective oral inhibitor of KIT and PDGFRA mutant kinases. It is a type 1 inhibitor designed to target the active kinase conformation; all oncogenic kinases signal via this conformation. Avapritinib has demonstrated broad inhibition of KIT and PDGFRA mutations associated with gastrointestinal stromal tumors (GIST), and the most potent activity against activation loop mutations, which currently approved therapies for GIST do not inhibit. In contrast with existing multi-kinase inhibitors, avapritinib has shown marked selectivity for KIT and PDGFRA over other kinases. In addition, avapritinib is uniquely designed to selectively bind and inhibit D816V mutant KIT, the primary driver of disease in approximately 90 to 95 percent of all SM patients. Preclinical studies have shown avapritinib potently inhibited KIT D816V at sub-nanomolar potencies with minimal off-target activity.

Blueprint Medicines is initially developing avapritinib, an investigational medicine, for the treatment of advanced GIST, advanced SM, and indolent and smoldering SM. The U.S. Food and Drug Administration has granted avapritinib two Breakthrough Therapy Designations, one for the treatment of PDGFRα D842V-driven GIST and one for advanced SM.

Blueprint Medicines has an exclusive collaboration and license agreement with CStone Pharmaceuticals for the development and commercialization of avapritinib and certain other drug candidates in Mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains development and commercial rights for avapritinib in the rest of the world.

About Blueprint Medicines

Blueprint Medicines is 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 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 the ongoing Phase 1 EXPLORER clinical trial, ongoing Phase 2 PATHFINDER clinical trial and planned Phase 2 PIONEER clinical trial; expectations regarding the potential for the Phase 1 EXPLORER clinical trial, Phase 2 PATHFINDER clinical trial or Phase 2 PIONEER clinical trial to be registration-enabling for avapritinib in SM; 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 advanced, indolent and smoldering SM; expectations regarding the development of avapritinib as a treatment for patients with SM, including advanced, indolent and smoldering SM; expectations regarding the potential for expedited 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 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 avapritinib for PDGFRα D842V-driven GIST, BLU-554 for FGFR4-driven hepatocellular carcinoma 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 September 30, 2018, as filed with the Securities and Exchange Commission (SEC) on October 30, 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, a Potent and Selective Inhibitor of KIT D816V, Improves Symptoms of Advanced Systemic Mastocytosis (AdvSM)

Analyses of Patient Reported Outcomes (PROs) from the Phase 1 (EXPLORER) Study Using the AdvSM Symptom Assessment Form (AdvSM-SAF), a New PRO Questionnaire for AdvSM

Jason Gotlib, Deepti Radia, Daniel J. DeAngelo, Prithviraj Bose, Mark W Drummond, Elizabeth O. Hexner, William A. Robinson, Maureen G. Conlan, Ronny Oren, Hongliang Shi and Michael W. Deininger

EXPLORER Advanced SM

American Society of Hematology Annual Meeting
San Diego, CA, 2 Dec 2018

Systemic mastocytosis (SM) is a rare heterogenous clonal mast cell disorder driven by *KIT* D816V mutation

ADVANCED SM (AdvSM)

Mast cell leukemia (MCL)	SM with an associated hematological neoplasm (SM-AHN)	Aggressive SM (ASM)	Smoldering SM (SSM)	Indolent SM (ISM)

Decreased Life Expectancy

Organ Involvement and/or Damage

Debilitating Patient Symptoms

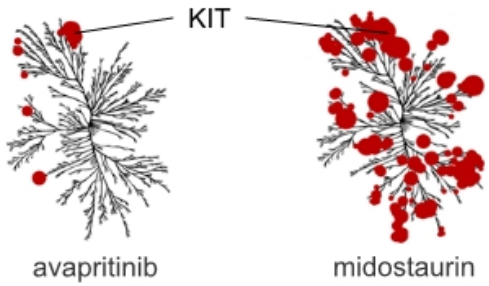
KIT D816V mutation in 90-95% of all subtypes

LIMITED TREATMENT OPTIONS

Multi-kinase inhibitor midostaurin	No approved therapies for ISM/SSM
Supportive care: anti-histamines, corticosteroids, cromolyn, leukotriene receptor antagonists	

Avapritinib was designed to target KIT D816V

Potent and highly selective inhibitor of D816V mutant *KIT*



KIT D816V biochemical IC_{50}	
0.27 nM	2.9 nM

Evans EK et al. Sci Transl Med. 2017;9(414)

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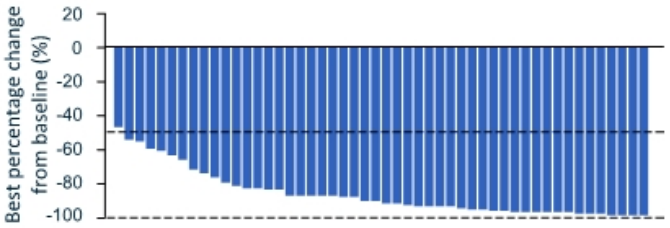
Clinical proof-of-concept in Phase 1 EXPLORER clinical trial[1-3]

m-IWG-MRT-ECNM ORR: 83%[2*]

Serum tryptase reduction in all patients[2]



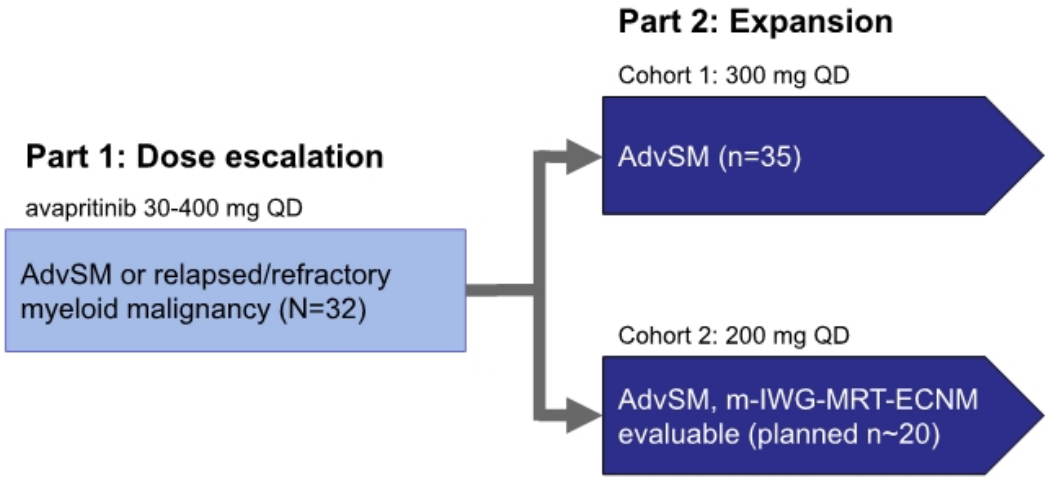
1. DeAngelo et al. ASH 2017 (Plenary Session)
2. Deininger et al. EHA 2018
3. Gotlib et al. ECNM 2018

Granted FDA Breakthrough Therapy Designation for AdvSM

m-IWG-MRT-ECNM, modified International Working Group Myeloproliferative Neoplasms Research and Treatment and European Competence Network on Mastocytosis criteria; ORR, overall response rate

*Data previously reported at EHA 2018. Data cutoff date: April 30, 2018,

Phase 1 EXPLORER clinical trial design



Study objectives:
RP2D, safety, ORR per m-IWG-MRT-ECNM, patient-reported outcomes

All data in this presentation are based on a cut-off of September 30, 2018, unless otherwise noted; QD, once daily
RP2D, recommended Phase 2 dose

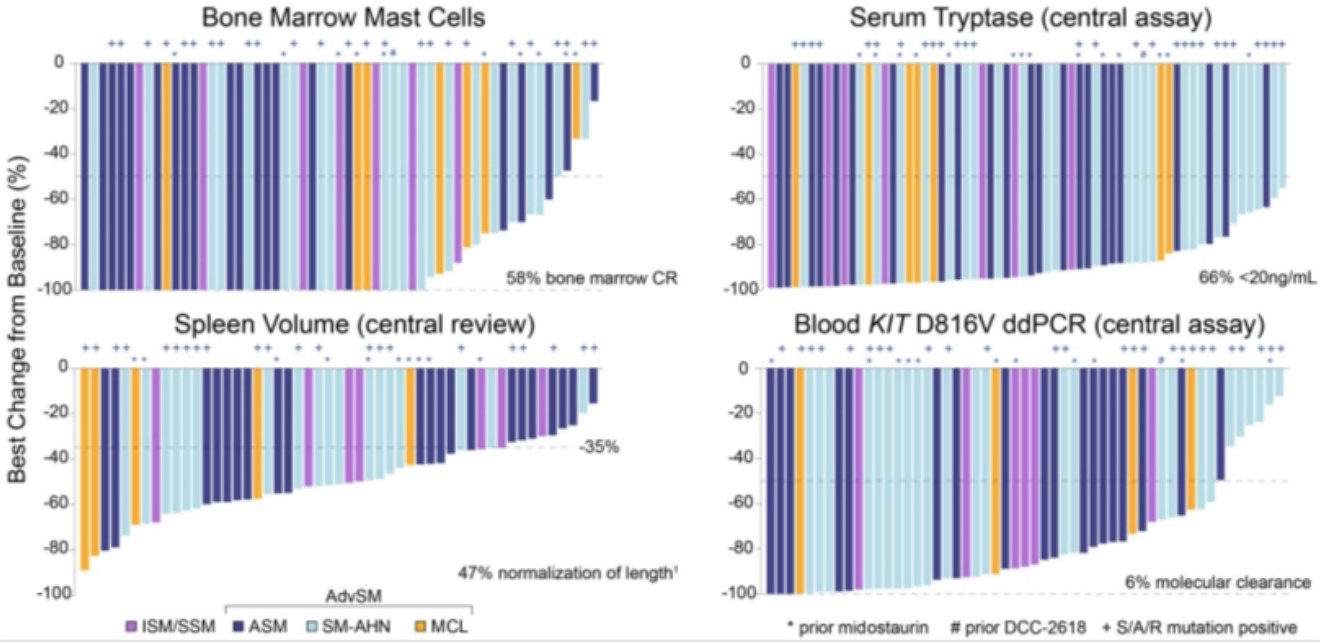
EXPLORER Advanced SM

Baseline characteristics

Parameter		All patients (N=67)
Median age, years (range) / Female, n (%)		62 (34 – 83) / 33 (49)
SM subtype per central assessment, n (%)*	AdvSM ASM SM-AHN MCL ISM/SSM	60 (90) 23 (34) 30 (45) 7 (10) 7 (10)
ECOG performance status, n (%)	0-1 2-3	50 (75) 17 (25)
KIT mutation, n (%)	D816V D816Y Wild-type	56 (84) 1 (1) 10 (15)
SRSF2, *ASXL1* and/or *RUNX1* mutation positive, n (%), n=64		29 (45)
Prior anti-neoplastic therapy	Median # of therapies (range) Any, n (%) Midostaurin	1 (0 – 3) 40 (60) 14 (23)
Baseline steroid therapy for SM		22 (33)
Bone marrow mast cell (MC) burden (%), median (range), n=65		30 (2 – 95)
Serum tryptase (µg/L), median (range), n=64		161 (13 – 1414)
Evaluable* by mIWG-MRT-ECNM criteria, n (% of AdvSM)		29 (48)

*Central adjudication of AdvSM with mIWG-MRT-ECNM C-finding(s) and at least 25 weeks follow up
ECOG: Eastern Cooperative Oncology Group

Decline in mast cell burden across subtypes, regardless of prior therapy or co-mutation status



¹by imaging or non-palpable

mIWG-MRT-ECNM responses are durable and deepen over time

Best response* n (%)	All doses (n=29)	≤200mg[1] QD (n=10)
ORR (CR + CRh + PR + CI)	**24 (83%)**	**9 (90%)**
Complete response (CR)	3 (10%)	3 (30%)
CR, partial hematologic recovery[2] (CRh)	4 (14%)	2 (20%)
Partial response (PR)	14 (48%)	3 (30%)
Clinical improvement (CI)	3 (10%)	1 (10%)
Stable disease (SD)	5 (17%)	1 (10%)
Progressive disease (PD)	0	0

- Ongoing treatment durations of up to 31 months (range 1+ to 31+)
- Median duration of response (DOR) not reached (median follow up 14 months)
- 12 month duration of response rate is 76%
- Median time to initial response is 2 months
- Median time to CR/CRh is 9 months

[1] started at ≤200mg QD. 90% have not dose escalated above 200mg as of the data cutoff date
[2] CRh: Requires all criteria for CR be met and response duration must be ≥12 weeks (to be confirmed); however, patient may have residual cytopenias. The following are required for CRh: ANC > 0.5 × 10^9/L with normal differential (absence of neoplastic MCs and blasts < 1%) *and* Platelet count > 50 × 10^9/L *and* Hgb level > 8.0 g/dL
*Pending confirmation: 3 transitioning from confirmed response to a deeper response, 3 transitioning from SD to first response

Treatment-emergent adverse events (AEs)

Adverse event, n (%)	Any Grade	Grade 3/4
NON-HEMATOLOGICAL AEs >15% (N=67)		
Periorbital edema	45 (67)	3 (4)
Fatigue	25 (37)	5 (7)
Nausea	24 (36)	3 (4)
Diarrhea	23 (34)	1 (1)
Peripheral Edema	23 (34)	0
Vomiting	19 (28)	2 (2)
Cognitive effects*	19 (28)	1 (1)
Hair color changes	17 (25)	1 (1)
Arthralgia	13 (19)	1 (1)
Dizziness	13 (19)	1 (1)
Abdominal pain	12 (18)	1 (1)
HEMATOLOGICAL AEs >10% (N=67)		
Anemia	35 (52)	18 (26)
Thrombocytopenia	21 (31)	12 (17)
Neutropenia	8 (12)	7 (10)

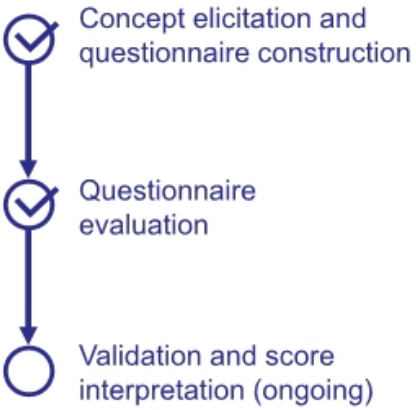
AEs of note: ascites (n=4 [6%]; n=1 [1%] at ≥ grade 3), pleural effusion (n=5 [7%], n=0 at ≥ grade 3),
*Cognitive effects include: cognitive disorder, confusional state, and memory impairment

- Most AEs were grade 1 or 2
- No treatment-related grade 5 AEs
- 4% (3/67) of patients discontinued due to treatment-related AEs
  - Refractory ascites, encephalopathy and intracranial bleed
- 66% (44/67) of patients had ≥ grade 3 treatment-related AEs and dose reduced
  - Most commonly hematologic AEs, typically in patients with prior cytopenias
  - Most dose reductions occurred at ≥300mg QD
- 78% (52/67) remain on treatment

AdvSM-SAF, first PRO tool designed specifically to assess AdvSM symptoms

Design and Validation

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



Symptom Assessment Form (SAF)

(all scores analyzed as last 7 days moving average)

Symptom	Domains	Score
Abdominal pain	GI domain	0-10 scored daily
Diarrhea		
Nausea		
Vomiting		
Spots	Skin domain	
Itching		
Flushing		
Fatigue		

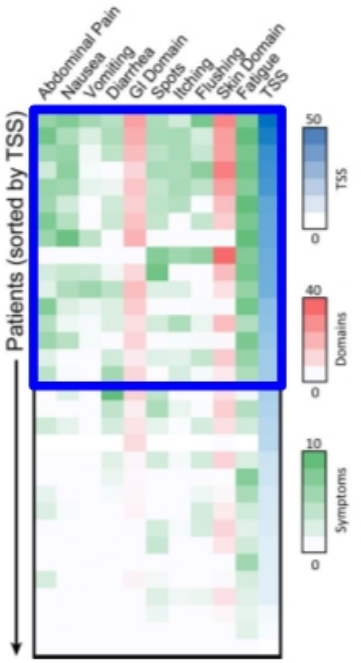
Total Symptom Score (TSS)

PRO: patient reported outcome

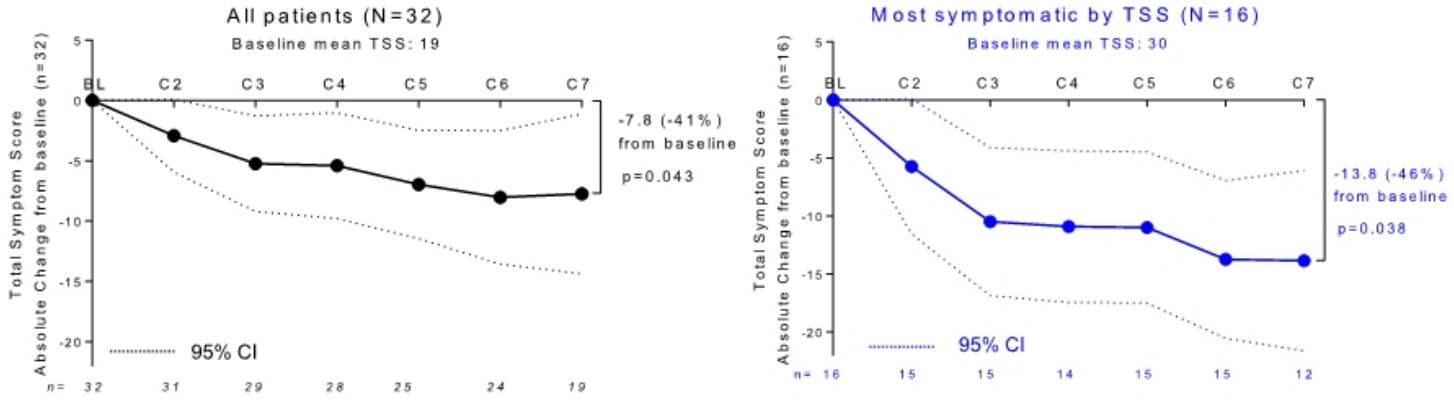
[1]Taylor et al. ISPOR 2017

Baseline AdvSM-SAF scores are heterogeneous

Symptom	Domains	All patients (n=32) Mean (range)	Most symptomatic Top 50th percentile TSS (n=16) Mean (range)
Abdominal pain	GI domain	3 (0-9)	5 (0-9)
Diarrhea		2 (0-10)	3 (0-6)
Nausea		2 (0-10)	4 (0-10)
Vomiting		1 (0-6)	2 (0-6)
Spots	Skin domain	3 (0-9)	4 (0-9)
Itching		2 (0-6)	3 (0-6)
Flushing		2 (0-9)	3 (0-9)
Fatigue		6 (0-10)	8 (5-10)
Total symptom score (TSS)		19 (0-50)	30 (18-50)



Avapritinib improves overall mastocytosis symptoms

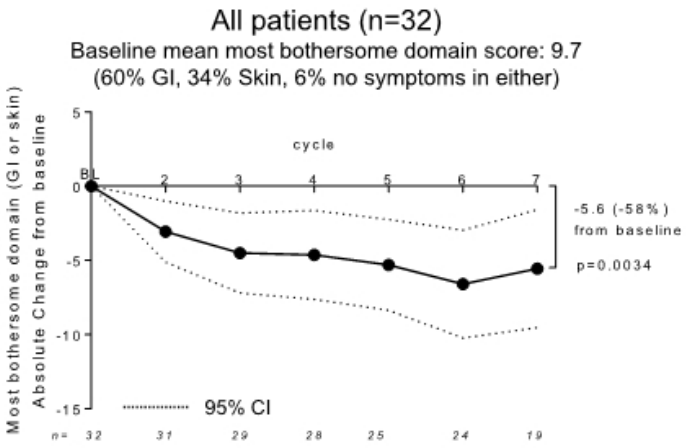


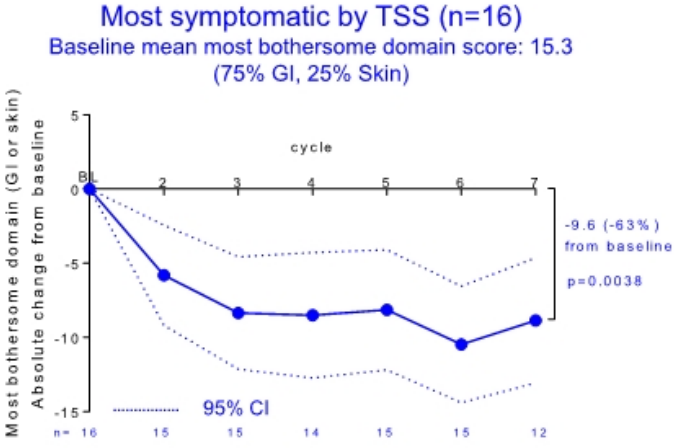
~40% mean reduction of symptoms from baseline TSS

Of 22 patients with baseline steroids for mastocytosis (parts 1 and 2):

- *18/22 (80%) decreased their steroid dose on study*
- *9/22 (41%) discontinued their steroids entirely on study*

Avapritinib improves most bothersome symptom domain

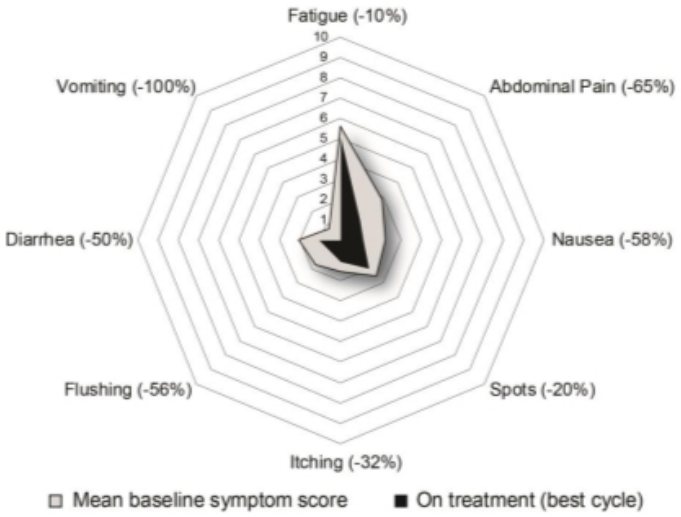




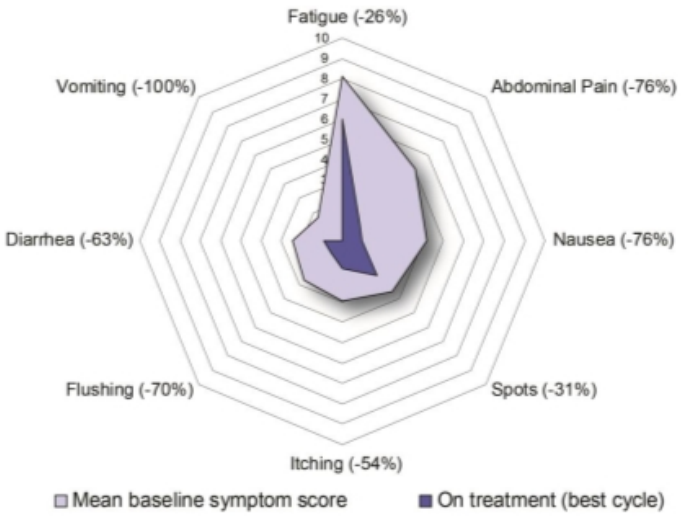
~60% mean reduction from baseline in most bothersome domain (GI or skin)

Avapritinib reduces individual mastocytosis symptoms

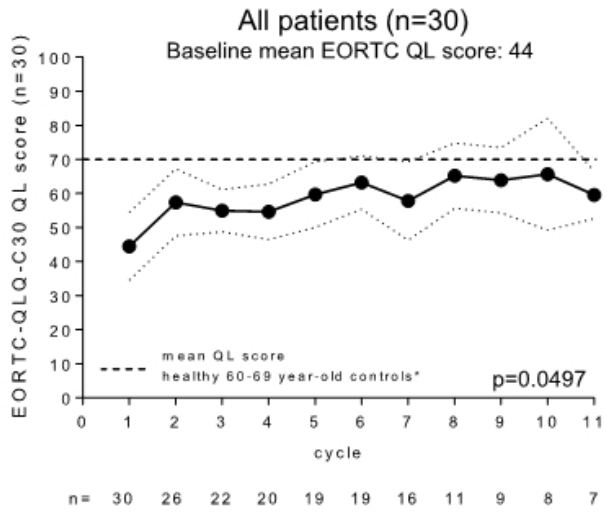
All patients (n=32)

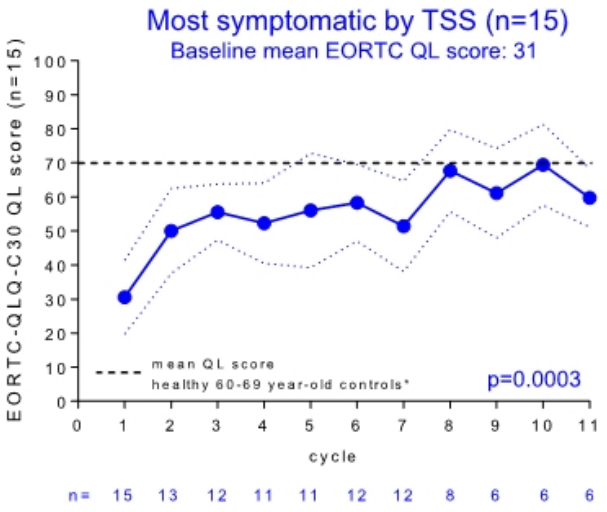


Most symptomatic by TSS (n=16)



Avapritinib improves quality of life of mastocytosis patients

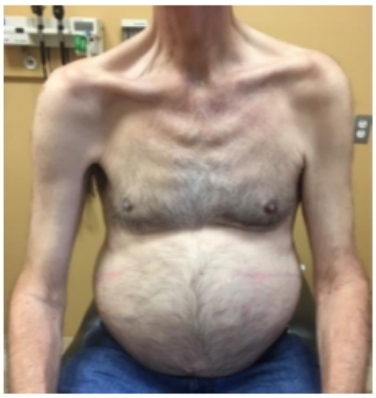




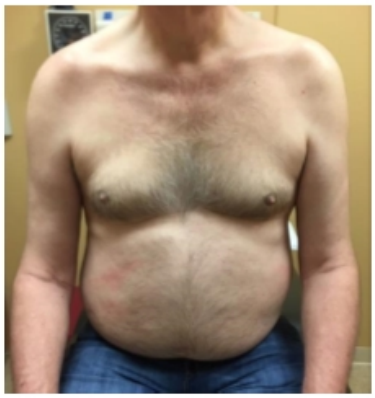
Significant improvement in EORTC quality of life (QL), approaching healthy age-matched controls

*Reference mean QL score from Hinz et al. Acta Oncologica. 2014

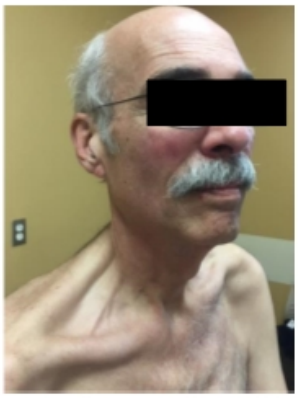
61 year old male with SM-AHN (CMML-1)



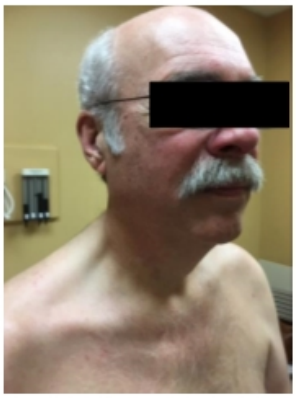
Baseline



Cycle 6 day 1



Baseline



Cycle 6 day 1

Prior therapy: DCC-2618

- Paracentesis-dependent ascites significantly improved on avapritinib 2 taps/week for 15L of fluid/week, now taps every 2-3 weeks and only 2-3L
- Albumin from 2.3 g/dL (G2) to 4 g/dL (normal)
- Gained 37 pounds of weight (not fluid) on study
- Tryptase from 416 ng/mL to 19.8 ng/mL
- Marrow mast cells from 30% to 5-10% after 2 cycles

Patient reported outcomes from AdvSM-SAF

Symptom improvement from baseline to cycle 6

- TSS -38% change (9.1 to 5.7)
- GI domain -69% change (1.9 to 0.6)
- Skin domain -47% change (2.1 to 1.1)

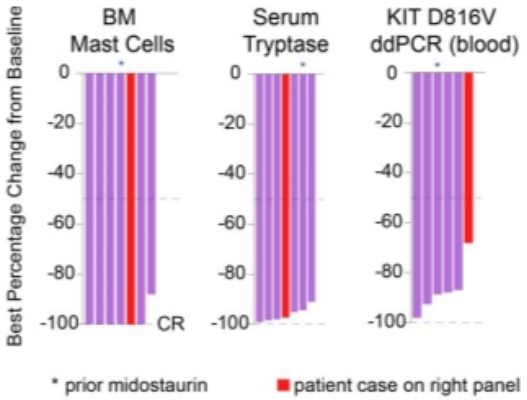
Data as of November 26, 2018

Patient permission granted for use of photos

ISM/SSM patient cohort from EXPLORER trial

All evaluable patients with ISM/SSM

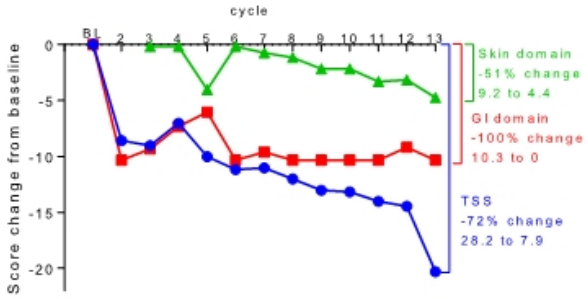
Objective measures of mast cell burden



All patients ongoing, median of 10 months

Case: 64-year-old woman with ISM

AdvSM-SAF total symptom score and domain scores



- Improvement in abdominal pain
- Confluent cutaneous lesions resolving
- Patient is continuing treatment on study

Avapritinib reduces objective signs and patient symptoms of SM

Summary

- High response rate and durable clinical benefit in patients with AdvSM
  - 83% ORR by mIWG-MRT-ECNM (24% CR + CRh)
  - Median duration of response not reached
- Well tolerated with most AEs grade 1 or 2; 78% remain on study, up to 31 months ongoing
- First AdvSM specific PRO demonstrates significant improvement in total symptom score
- Significant improvement in EORTC quality of life, approaching healthy age-matched controls
- Clinical activity and initial PRO data support further evaluation in both AdvSM and ISM/SSM
  - PATHFINDER trial in AdvSM now enrolling
  - PIONEER trial in ISM/SSM planned to initiate by end of 2018

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EXPLORER Advanced SM