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): **November 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 November 15, 2018, Blueprint Medicines Corporation (the "Company") issued a press release announcing updated data from its ongoing Phase 1 NAVIGATOR clinical trial evaluating avapritinib for the treatment of advanced gastrointestinal stromal tumors. The data will be presented on Thursday, November 15, 2018 in an oral presentation at the Connective Tissue Oncology Society 2018 Annual Meeting ("CTOS Annual Meeting") in Rome, Italy. 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 CTOS Annual Meeting is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

In addition, on November 15, 2018, the Company hosted an investor call and live webcast to discuss the data presented at the CTOS Annual Meeting. A copy of the presentation from the investor 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 November 15, 2018
99.2	Presentation by Blueprint Medicines Corporation at the CTOS Annual Meeting on November 15, 2018
99.3	Presentation by Blueprint Medicines Corporation at investor call on November 15, 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: November 15, 2018

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

Blueprint Medicines Announces Updated NAVIGATOR Trial Results in Patients with Advanced Gastrointestinal Stromal Tumors Supporting Development of Avapritinib Across All Lines of Therapy

– 84% ORR in PDGFRα D842V GIST and 20% ORR in fourth-line or later GIST support plans to submit New Drug Application to FDA in the first half of 2019 –

– 26% ORR in regorafenib-naïve third- and fourth-line GIST and 25% ORR in second-line GIST strongly support clinical development in earlier lines of treatment –

– Blueprint Medicines to host investor conference call and webcast on Thursday, November 15, 2018 at 7:30 a.m. ET –

CAMBRIDGE, Mass., November 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 for the registration-enabling NAVIGATOR clinical trial of avapritinib, a potent and highly selective KIT and PDGFRA inhibitor in development for patients with advanced gastrointestinal tumors (GIST). The data showed that avapritinib was highly active across all lines of therapy for patients with PDGFRα D842V-driven GIST and in second-, third- and fourth-line for other GIST patients. In addition, avapritinib was well-tolerated with most adverse events (AEs) reported by investigators as Grade 1 or 2. These results will be presented today in an oral presentation at the Connective Tissue Oncology Society 2018 Annual Meeting in Rome, Italy.

The updated data from the ongoing Phase 1 NAVIGATOR trial support Blueprint Medicines' plans to submit a New Drug Application (NDA) in the first half of 2019 to the U.S. Food and Drug Administration (FDA) for the treatment of PDGFRA Exon 18 mutant GIST, which primarily includes patients with the D842V mutation, and fourth-line GIST. There are currently no approved or effective therapies in these patient populations. In patients with PDGFRα D842V-driven GIST, avapritinib demonstrated an objective response rate (ORR) of 84 percent and a 12-month duration of response (DoR) of 76 percent. In heavily pre-treated patients with fourth-line or later GIST, avapritinib demonstrated an ORR of 20 percent, tumor reductions in 60 percent of patients and a median DoR of 7.3 months. ORR and DoR per central radiographic review will be the primary endpoints for the NDA submission, consistent with regulatory precedent for accelerated approvals based on single-arm oncology studies. In addition, avapritinib demonstrated an ORR of 26 percent in regorafenib-naïve third- and fourth-line GIST and an ORR of 25 percent in second-line GIST. Patients with PDGFRα D842V-driven GIST were excluded from both of these populations.

"With an increased understanding of molecular drivers of GIST over the last decade, it is encouraging to see an investigational drug, like avapritinib, bring a precision therapy approach to GIST," said Michael Heinrich, M.D., Professor of Medicine at Oregon Health & Science University and an investigator on the NAVIGATOR trial. "Avapritinib has the potential to be a significant therapeutic advance in GIST, a rare cancer with high medical needs across lines of treatment. In particular, the updated data demonstrate the broad clinical impact of avapritinib for patients with PDGFRα D842V-driven GIST and fourth-line GIST, where there are currently no effective therapies. In addition, the data strongly support clinical development of avapritinib in early lines, including second- and third-line treatment."

“These data highlight the potential of avapritinib, a potent and highly selective inhibitor of KIT and PDGFRA mutant kinases, to be a cornerstone precision therapy in GIST,” said Andy Boral, M.D., Ph.D., Chief Medical Officer of Blueprint Medicines. “The results validate Blueprint Medicines’ approach to designing precision therapies that specifically target genetic drivers of disease, with the goals of delivering transformative benefit to patients and enabling rapid progress toward registration. Avapritinib’s highly potent anti-tumor activity in PDGFRα D842V-driven GIST, combined with differentiated activity across treatment lines in KIT-driven GIST, reflect its promise as a potentially foundational treatment option across multiple GIST populations. We are committed to advancing a comprehensive and scientifically driven clinical development program with the goal of improving the lives of GIST patients.”

Data Highlights from the Ongoing Phase 1 NAVIGATOR Clinical Trial

As of the data cutoff date of October 15, 2018, 231 patients were treated with avapritinib in the dose escalation and expansion portions of the Phase 1 clinical trial at eight dose levels, ranging from 30 mg once daily (QD) to 600 mg QD. This population consisted of 167 patients with KIT-driven GIST, 56 patients with PDGFRα D842V-driven GIST and eight patients with other PDGFRA mutations. Patients in the expansion portion of the clinical trial were treated at the recommended Phase 2 dose of 300 mg QD.

Safety Data

As of the data cutoff date, avapritinib was well-tolerated, and most AEs reported by investigators were Grade 1 or 2. Across all doses, 20 patients (8.7 percent) discontinued treatment with avapritinib due to treatment-related AEs.

Across all grades, the most common treatment-emergent AEs (regardless of relationship to avapritinib) reported by investigators (≥20 percent) included nausea (61 percent), fatigue (55 percent), anemia (46 percent), periorbital edema (40 percent), diarrhea (39 percent), vomiting (38 percent), decreased appetite (35 percent), peripheral edema (33 percent), increased lacrimation (31 percent), memory impairment (26 percent), constipation (23 percent), face edema (23 percent), hair color changes (21 percent) and dizziness (20 percent).

Investigator-reported Grade 3 or 4 treatment-related AEs (≥2 percent) included anemia, fatigue, hypophosphatemia, increased bilirubin, decreased white blood count/neutropenia and diarrhea.

Clinical Activity Data

As of the data cutoff date, the following patients were evaluable for response assessments: 56 patients with PDGFRα D842V-driven GIST, 109 patients with fourth-line or later GIST, 23 patients with third- or fourth-line GIST who did not receive prior regorafenib (which is comparable to the VOYAGER trial population) and do not harbor the PDGFRα D842V mutation, and 20 patients with second-line GIST who do not harbor the PDGFRα D842V mutation. Patients were evaluable if they had at least one centrally reviewed radiographic scan, and data are based on modified Response Evaluation Criteria in Solid Tumors version 1.1 (mRECIST 1.1 criteria) for GIST.

Across multiple lines of therapy, avapritinib demonstrated important clinical activity in patients with PDGFRA- and KIT-driven GIST.

GIST Population	Evaluable Patients	ORR	Clinical Benefit Rate at Four Months (≥Two Scans)	Median DoR	Median PFS Central Review (Investigator Review)
PDGFRα D842V[a]	56	84%[f]	96%	Not estimable; 76% at 12 months	Not reached
Fourth-line or later[b,c]	109	20%[g]	40%	7.3 months	3.7 months (5.4 months)
Regorafenib-naïve third- or fourth-line[b,d]	23	26%	70%	10.2 months	8.6 months (10.2 months)
Second-line[d,e]	20	25%[h]	NR[i]	NR[i]	NR[i]

Notes: (a) Treated at all doses; (b) Treated at doses of 300 or 400 mg QD; (c) Included patients with the PDGFRα D842V mutation, whose proportion was consistent with the known mutational prevalence in this GIST population; (d) Did not include patients with the PDGFRα D842V mutation, whose proportion was greater than the known mutational prevalence in this GIST population; (e) Treated at doses up to and including 300 or 400 mg QD; (f) Four PR pending confirmation; (g) One PR pending confirmation; (h) Three PR pending confirmation; (i) NR, not reported, as data are too early to estimate.

Additional Data Support Clinical Development Strategy in Earlier Lines of Therapy

Third- and Fourth-Line GIST

Preliminary data showed robust clinical activity in regorafenib-naïve third- and fourth-line GIST patients lacking the PDGFRα D842V mutation. As of the data cutoff date, the ORR was 26 percent, tumor reductions were demonstrated in 78 percent of patients, and the median PFS was 8.6 months per central radiographic review and 10.2 months per investigator review. In contrast, historical data showed a 5 percent ORR and a median PFS of 4.8 months for regorafenib, the current standard-of-care treatment in third-line GIST.

In regorafenib-naive patients with PDGFRα D842V-driven third- or fourth-line GIST, the ORR was 80 percent (eight out of 10 evaluable patients, with one response pending confirmation). Blueprint Medicines' ongoing Phase 3 VOYAGER trial of avapritinib versus regorafenib in third- or fourth-line GIST permits enrollment of patients with both KIT- and PDGFRA-driven GIST, including patients with the PDGFRα D842V mutation. Blueprint Medicines anticipates completing enrollment of the VOYAGER trial in the second half of 2019.

Second-Line GIST

Preliminary data showed a 25 percent ORR in second-line GIST, excluding patients with the PDGFRα D842V mutation. In patients with second-line PDGFRα D842V-driven GIST, the ORR was 94 percent (15 out of 16 evaluable patients, with two responses pending confirmation).

In addition, analyses of circulating tumor DNA (ctDNA) from the NAVIGATOR trial across all lines showed increased activity for avapritinib in patients without the secondary KIT V654A or T670I mutations, which are estimated to occur in about 20 to 25 percent of GIST patients following treatment with imatinib (second-line or later). Independently published data for sunitinib, the current standard of care therapy for second-line GIST, have shown activity against these mutations.

Based on the totality of data, Blueprint Medicines believes a precision medicine approach has the potential to optimize patient outcomes in second-line GIST. The company plans to initiate the registration-enabling Phase 3 COMPASS-2L clinical trial in the second half of 2019 using a ctDNA-guided patient selection strategy. The planned trial will select patients with PDGFRA- and KIT-driven second-line GIST who do not have the KIT V654A or T670I mutations, and randomize them to receive avapritinib or sunitinib with an anticipated primary endpoint of PFS.

Conference Call Information

Blueprint Medicines will host a live conference call and webcast on November 15, 2018 at 7:30 a.m. ET to review the updated data for avapritinib in GIST. The conference call may be accessed by dialing (855) 728-4793 (domestic) or (503) 343-6666 (international) and referring to conference ID 3479587. A live webcast of the conference call will be available under “Events and Presentations” in the Investors section of Blueprint Medicines’ website at http://ir.blueprintmedicines.com. The archived webcast will be available on Blueprint Medicines’ website approximately two hours after the conference call and will be available for 30 days following the call.

About the Avapritinib Clinical Development Program in GIST

Blueprint Medicines is pursuing a broad clinical development program for avapritinib across all lines of GIST. Avapritinib is currently being evaluated in two ongoing registration-enabling clinical trials for GIST: the Phase 1 NAVIGATOR trial and the Phase 3 VOYAGER trial.

The NAVIGATOR trial is designed to evaluate the safety and tolerability of avapritinib in patients with advanced GIST. The trial consists of two parts, a dose escalation portion and an expansion portion. The dose escalation portion is complete, and trial objectives include assessing response, pharmacokinetics and pharmacodynamic measures. Response assessments use blinded, central radiology review. The expansion cohorts of the trial are designed to enroll a total of approximately 200 patients at multiple sites in the United States, United Kingdom and European Union.

The VOYAGER trial is a global, open-label, randomized, Phase 3 trial designed to evaluate the safety and efficacy of avapritinib versus regorafenib in patients with third- or fourth-line advanced GIST. The trial is designed to enroll approximately 460 patients randomized 1:1 to receive either avapritinib or regorafenib at multiple sites in the United States, United Kingdom, European Union, Australia and Asia.

In the second half of 2019, Blueprint Medicines plans to initiate COMPASS-2L, a global, randomized, Phase 3 precision medicine trial. The trial will evaluate the safety and efficacy of avapritinib versus sunitinib in patients with second-line advanced GIST and pre-specified disease genotypes.

Patients and physicians interested in the Phase 3 VOYAGER trial can contact the Blueprint Medicines study director at VOYAGER@blueprintmedicines.com or 1-617-714-6707. For more information about

the VOYAGER trial, please visit www.voyagertrial.com. Additional details are available on www.clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT03465722).

About GIST

GIST is a sarcoma, or tumor of bone or connective tissue, of the gastrointestinal (GI) tract. Tumors arise from cells in the wall of the GI tract and occur most often in the stomach or small intestine. Most patients are diagnosed between the ages of 50 to 80, and diagnosis is typically triggered by GI bleeding, incidental findings during surgery or imaging and, in rare cases, tumor rupture or GI obstruction.

Most GIST cases are caused by a spectrum of clinically relevant mutations that force the KIT or PDGFRA protein kinases into an increasingly active state. Because currently available therapies only bind to the inactive protein conformations, certain primary and secondary mutations typically lead to treatment resistance and disease progression.

Treatment options for KIT-driven GIST patients whose disease progresses or develops resistance are currently limited. There are no effective treatment options for patients with PDGFRA-driven GIST, and progression often occurs in as little as three months with available therapies. In advanced GIST, clinical benefits from existing treatments can vary by mutation type. Early testing is critical to help guide therapy that effectively treats the underlying driver of disease and is recommended in expert guidelines.

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 GIST, and the most potent activity against activation loop mutations, which currently approved therapies 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 bind and inhibit the KIT D816V mutation, the primary driver of disease in up to 95 percent of systemic mastocytosis (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 FDA 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 initiating the Phase 3 COMPASS-2L trial and completing enrollment in the Phase 3 VOYAGER trial; expectations regarding the potential benefits of avapritinib in treating patients with GIST; plans and timelines for submitting an NDA to the FDA for avapritinib for the treatment of PDGFRA Exon 18 mutant GIST and fourth-line GIST; 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 is Highly Active and Well-tolerated in Patients With Advanced GIST Driven by a Diverse Variety of Oncogenic Mutations in KIT and PDGFRA

Michael Heinrich, Margaret von Mehren, Robin L. Jones, Sebastian Bauer, Yoon-Koo Kang, Patrick Schöffski, Ferry Eskens, César Serrano, Philippe A. Cassier, Olivier Mir, William D. Tap, Piotr Rutkowski, Jonathan Trent, Shreyaskumar Patel, Sant P. Chawla, Teresa Zhou, Tamieka Lauz, Oleg Schmidt-Kittler, Khalid K. Mamlouk, Beni B. Wolf, Suzanne George

Connective Tissue Oncology Society 2018 Annual Meeting
Rome, Italy • November 15, 2018

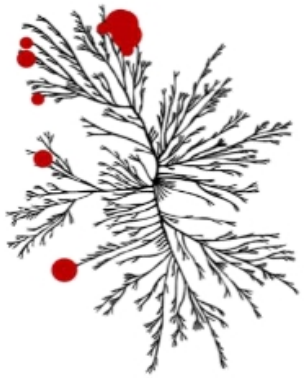
Abstract no: 3027631

Disclosures

- Avapritinib is an investigational agent discovered and currently in development by Blueprint Medicines Corporation (Blueprint Medicines)
- Data are preliminary and based on a cutoff date of October 15, 2018
- Dr. Michael Heinrich is an investigator for Blueprint Medicines' ongoing Phase 1 study in unresectable gastrointestinal stromal tumors
- Dr. Michael Heinrich has the following disclosures:
  - Consultant: Blueprint Medicines, Novartis, Molecular MD, Deciphera
  - Research funding: Blueprint Medicines, Deciphera
  - Stock or stock options: Molecular MD
  - Patents: 4 patents on diagnosis and treatment of PDGFRα-mutant GIST, 1 patent on imatinib treatment of GIST

Avapritinib: a highly selective and potent KIT/PDGFRA inhibitor for GIST

GIST mutation(s)		Medical need by mutation	Avapritinib biochemical IC_{50}[1]
KIT Exon 11 deletion	JM domain	1L imatinib is effective 2L sunitinib/3L regorafenib have low ORR/short PFS	0.6 nM
KIT Exon 11 V560G			1 nM
KIT Exon 11/13	ATP binding site	Approved 2L/3L agents have low ORR/short PFS	11 nM
KIT Exon 11/14			28 nM
KIT Exon 11/17	Activation loop		0.1 nM
PDGFRα D842V		No highly effective therapy in any line	0.24 nM



Avapritinib kinome selectivity

Ongoing clinical trials

NAVIGATOR GIST

Phase 1 advanced GIST

VOYAGER GIST

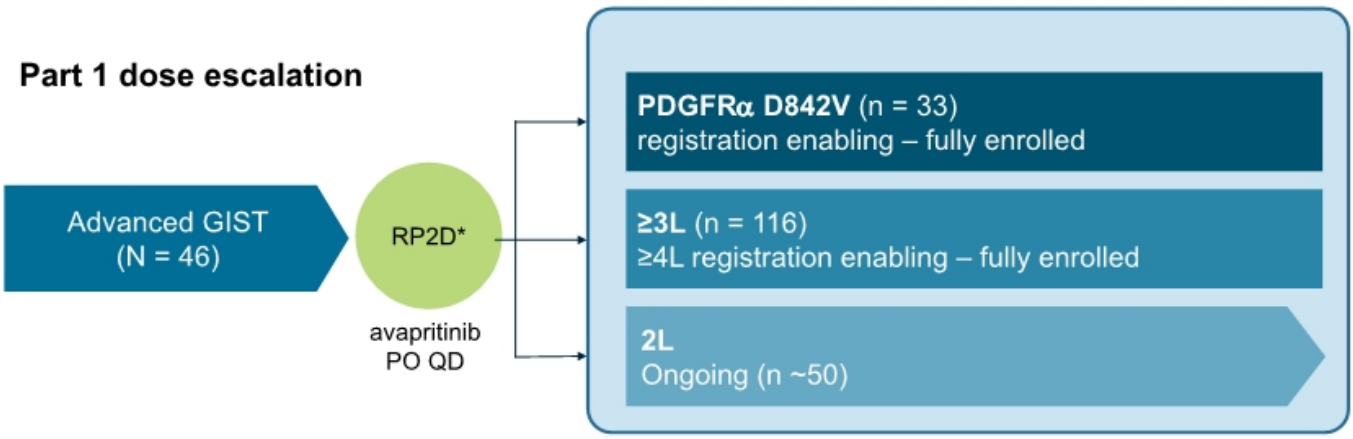
Phase 3 trial of avapritinib vs. regorafenib in 3L and 4L GIST

KIT, KIT proto-oncogene receptor tyrosine kinase; PDGFRA, platelet-derived growth factor alpha; IC_{50}, concentration causing 50% inhibition; L, line; JM, juxtamembrane; ORR, objective response rate; PFS, progression-free survival.

Kinome illustrations reproduced courtesy of Cell Signaling Technology, Inc. (CSTI) (www.cellsignal.com). Blueprint Medicines is not responsible for the content of the CSTI site.

[1]Evans E, et al. Sci Transl Med. 2017;9(414). pii: eaao1690.

NAVIGATOR Phase 1 study design



KEY OBJECTIVES

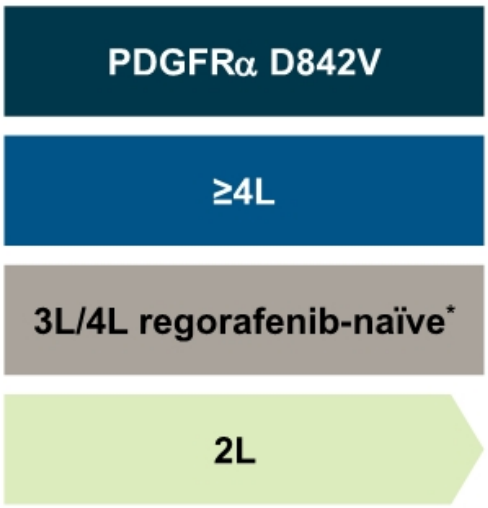
- Determine MTD/RP2D, safety, PK and clinical activity by line of therapy and mutational status
- ORR/DOR per central radiology assessment (mRECIST 1.1) for planned NDA and MAA regulatory filings

RP2D, recommended Phase 2 dose; PO, orally; QD, once daily; MTD, maximum tolerated dose; PK, pharmacokinetics; DOR, duration of response; mRECIST, modified Response Evaluation Criteria in Solid Tumors; NDA, New Drug Application; MAA, Marketing Authorization Application.
*MTD 400 mg; RP2D 300 mg.

Demography and baseline characteristics

Parameter	All patients (N = 231)	
Age (years), median (range)	62 (25, 90)	
GIST mutational subtype, % (n) KIT PDGFRα D842V PDGFRα non-D842V	 72% (167) 24% (56) 4% (8)	
Metastatic disease, % (n)	89% (205)	
Largest target lesion size, % (n) ≤5 cm >5–≤10 cm >10 cm Pending	 34% (79) 40% (93) 20% (47) 5% (12)	
No. prior kinase inhibitors, % (n) Median (range) 0 1 2 3 4 ≥5	<u>PDGFRα</u> 1 (0-6) 17% (11) 37% (24) 19% (12) 11% (7) 8% (5) 8% (5)	<u>KIT</u> 4 (1-11) 0 19% (31) 8% (14) 20% (34) 23% (38) 30% (50)

Efficacy populations



*Similar to Phase 3 trial population (VOYAGER).
Data are preliminary and based on a cutoff date of October 15, 2018.

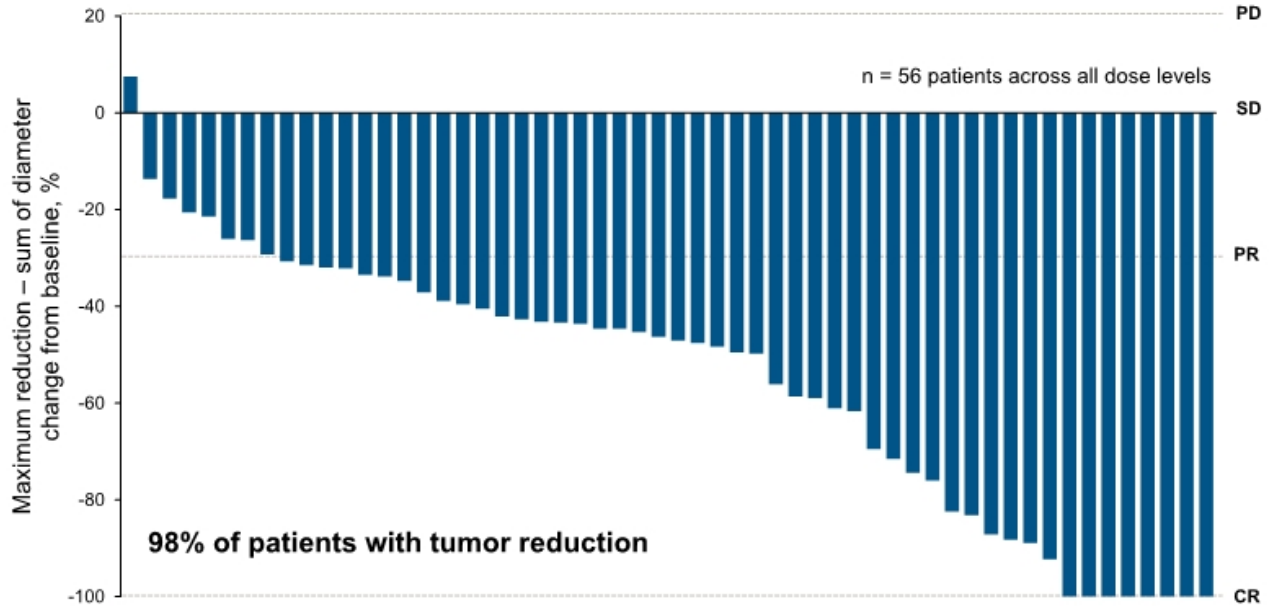
Adverse events ≥20%

Safety population; all doses (N = 231)					
AE, % (n)	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4
Nausea	61% (142)	46% (106)	13% (30)	3% (6)	0
Fatigue	55% (127)	21% (48)	28% (64)	6% (15)	0
Anemia	46% (107)	5% (11)	15% (35)	25% (58)	1% (3)
Periorbital edema	40% (93)	34% (79)	6% (13)	<1% (1)	0
Diarrhea	39% (90)	22% (50)	13% (30)	4% (10)	0
Vomiting	38% (88)	30% (69)	6% (14)	2% (5)	0
Decreased appetite	35% (82)	23% (54)	9% (20)	3% (8)	0
Peripheral edema	33% (77)	23% (53)	10% (22)	<1% (2)	0
Increased lacrimation	31% (72)	28% (64)	3% (8)	0	0
Memory impairment*	26% (60)	19% (45)	6% (15)	0	0
Constipation	23% (53)	14% (32)	8% (18)	<1% (2)	<1% (1)
Face edema	23% (53)	19% (43)	4% (9)	<1% (1)	0
Hair color changes	21% (49)	20% (46)	<1% (2)	<1% (1)	0
Dizziness	20% (47)	16% (38)	3% (8)	<1% (1)	0

AE, adverse event.
*The most commonly reported cognitive AE

- Most AEs are grade 1 or 2
- No treatment-related grade 5 AEs
- 8.7% (20) of patients discontinued due to related AEs
- Grade 3-4 treatment-related AEs ≥2%: anemia, fatigue, hypophosphatemia, increased bilirubin, decreased white blood count/neutropenia, and diarrhea

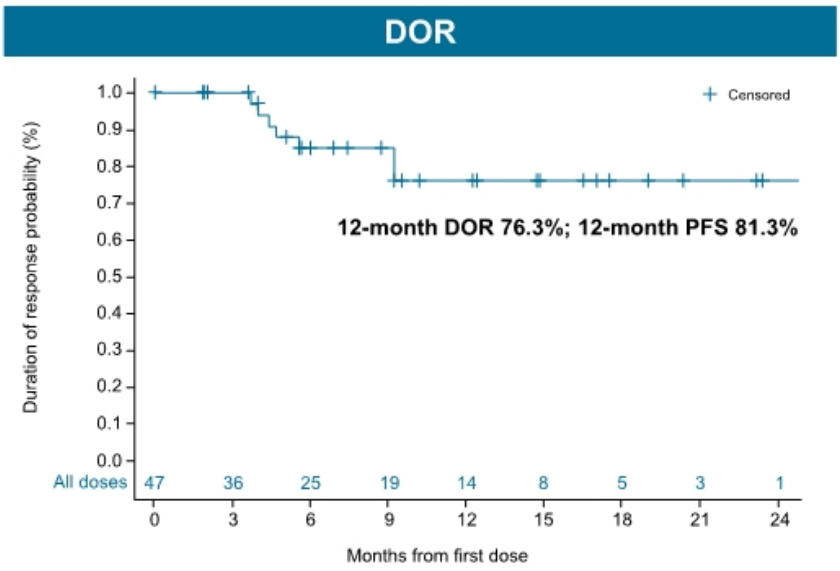
Best response by central radiology in PDGFRα D842V GIST



PD, progressive disease; SD, stable disease; PR, partial response; CR, complete response.

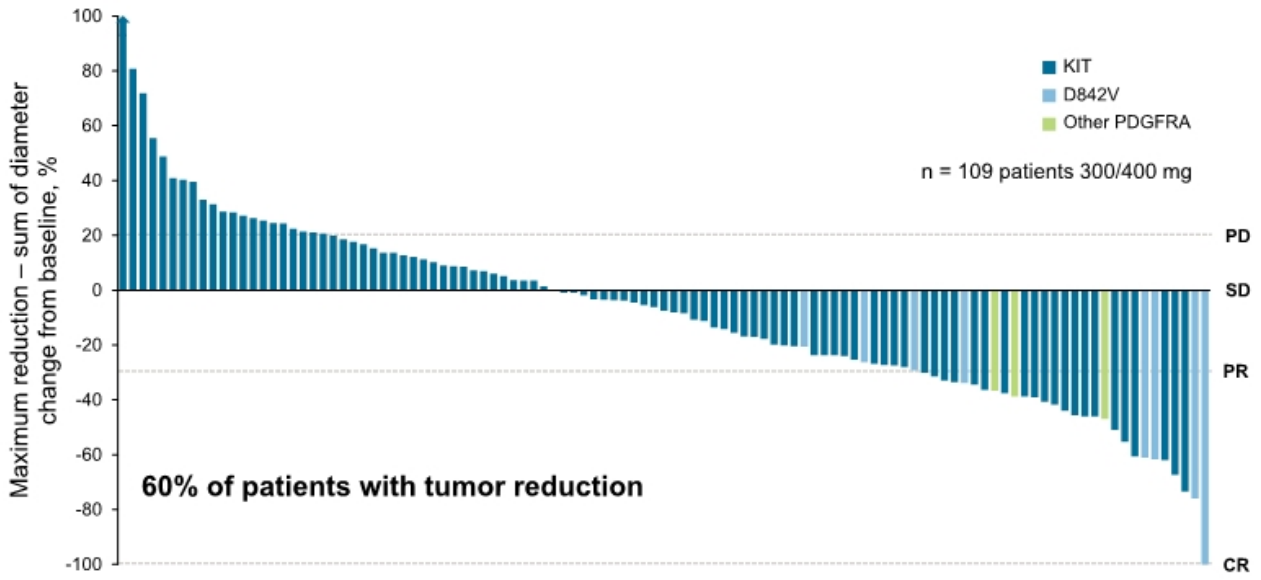
ORR and DOR by central radiology in PDGFRα D842V GIST

Best response* n = 56	mRECIST 1.1 % (n) [95% CI]
ORR	84% (47) [71.7-92.47]
CR/PR*	9% (5)/75% (42)
SD	16% (9)
CBR†	96% (54) [87.7-99.6]



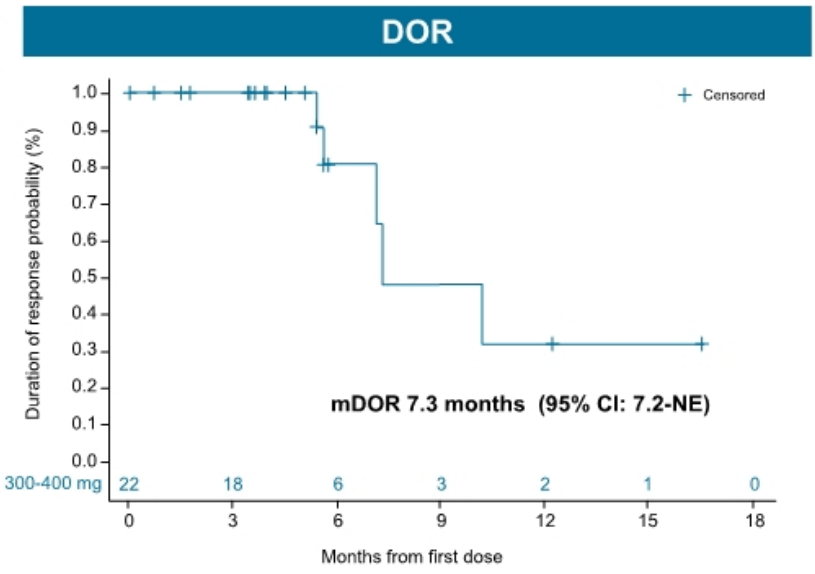
CI, confidence interval; CBR, clinical benefit rate.
*4 PR pending confirmation. Patients who have had ≥1 post-baseline radiographic assessment. Response evaluable includes all doses.
† PR + SD lasting ≥4 months.

Best response by central radiology in ≥4L GIST



ORR and DOR by central radiology ≥4L GIST

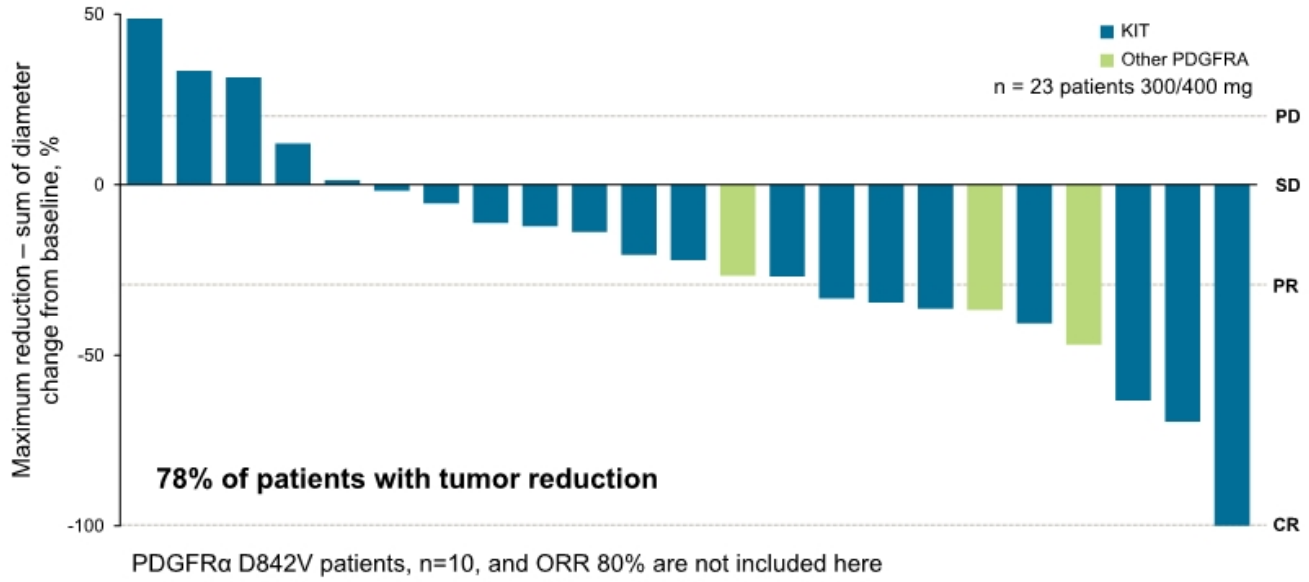
Best response* n = 109	mRECIST 1.1 % (n) [95% CI]
ORR	20% (22) [13.1-29.0]
CR/PR*	1% (1)/19% (21)
SD	46% (50)
CBR†	40% (44) [31.1-50.2]



mDOR, median duration of response; NE, not estimatable

*1 PR pending confirmation. Patients who have had ≥1 post-baseline radiographic assessment. Response evaluable includes 300 mg and 400 mg.
†PR + SD lasting ≥4 months

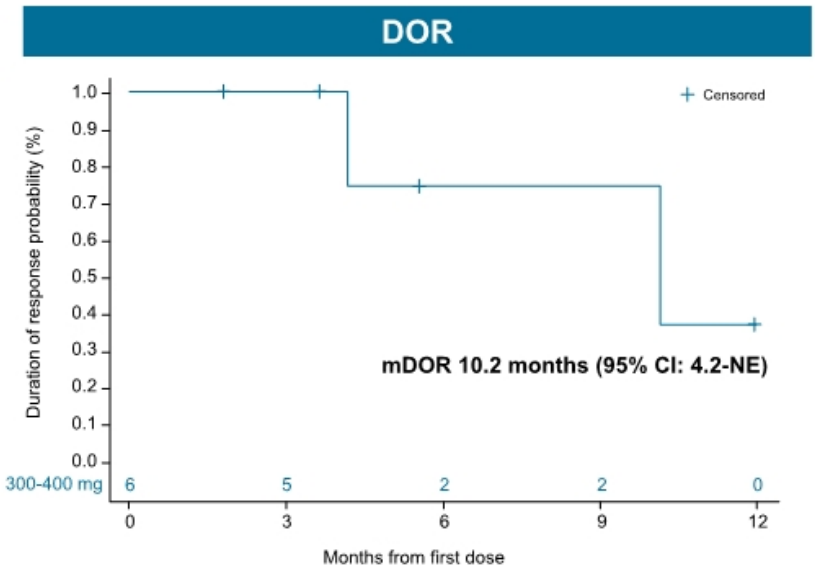
Best response by central radiology in 3L/4L regorafenib-naïve GIST*



*Similar to Phase 3 trial population (VOYAGER), except that PDGFRα D842V patients (ORR 80%) are not included here.

ORR and DOR by central radiology in 3L/4L regorafenib-naïve GIST

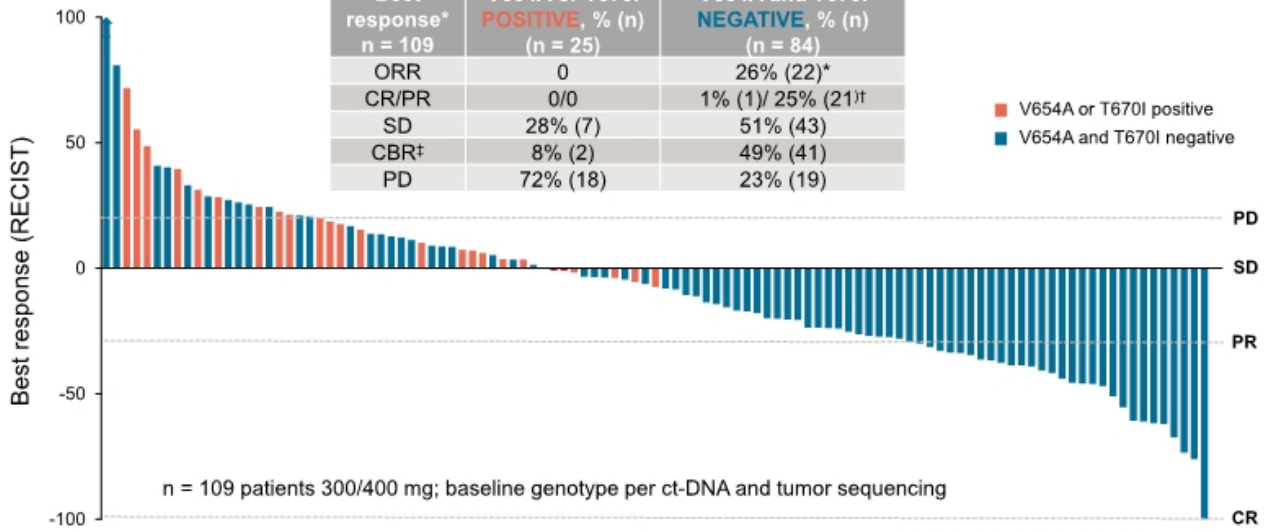
Non-D842V patients best response* n = 23	mRECIST 1.1 % (n) [95% CI]
ORR	26% (6) [10.0-48.4]
CR/PR	0% (0)/26% (6)
SD	57% (13)
CBR†	70% (16) [47.1-86.8]



*All responses are confirmed. Patients who have had ≥1 post-baseline radiographic assessment. Response evaluable includes 300 mg and 400 mg.
†PR + SD lasting ≥4 months

Best response by mutational profile in ≥4L GIST

Best response* n = 109	V654A or T670I POSITIVE, % (n) (n = 25)	V654A and T670I NEGATIVE, % (n) (n = 84)
ORR	0	26% (22)*
CR/PR	0/0	1% (1)/ 25% (21)†
SD	28% (7)	51% (43)
CBR‡	8% (2)	49% (41)
PD	72% (18)	23% (19)



ct-DNA, circulating tumor DNA.

*Patients who have had ≥1 post-baseline radiographic assessment. Response evaluable includes 300 mg and 400 mg.

† Includes 1 unconfirmed PR.

‡PR + SD lasting ≥4 months

Avapritinib has important clinical activity in advanced GIST

	PDGFRα D842V n = 56	≥4L all patients n = 109	3L/4L regorafenib-naïve non-D842V n = 23	2L non-D842V n = 20
ORR (central radiology), % (n) [95% CI]	84% (47) [72-92]	20% (22) [13.1-29.0]	26% (6) [10.2-48.4]	25% (5) [9-49]
mDOR (central radiology), months [95% CI]	NE [NE, NE]	7.3 [7.2-NE]	10.2 [4.2-NE]	NR
CBR (central radiology), % (n) [95% CI]	96% (54) [88-100]	40% (44) [31.1-50.2]	70% (16) [47.1-86.8]	NR
mPFS (central radiology), months [95% CI]	NE [NE, NE]	3.7 [3.5-5.6]	8.6 [5.6-14.7]	NR
mPFS (investigator), months [95% CI]	22.8 [20.8-28.4]	5.5 [3.8-6.8]	10.2 [5.7-NE]	NR
Benchmarks	**PDGFRα D842V** Approved agents: ORR ~0% mPFS ~3 mo mOS ~15 mo	**4L** imatinib re-treatment: ORR ~0% PFS 1.8 mo	**3L** regorafenib: ORR ~5% PFS 4.8 mo	**2L** sunitinib: ORR ~7% PFS 6 mo

NR, not reported; mPFS, median progression-free survival; mOS, median overall survival.

– – ORR is not an endpoint for 2L but is early signal readout.

Avapritinib has the potential to change GIST treatment paradigms

- Phase 1 NAVIGATOR study demonstrates favorable tolerability and encouraging clinical activity across lines of therapy
  - Most AEs were grade 1 or 2, with manageable on-target toxicity
  - Important efficacy in PDGFRα D842V GIST and refractory, ≥4L GIST supports regulatory filing
  - Encouraging activity in 3L/4L regorafenib-naïve GIST indicates the potential for a favorable outcome in the ongoing randomized Phase 3 VOYAGER study
  - Mutational profiling analyses and promising 2L data provide strong rationale for genotype-selected 2L study

Acknowledgments

We would like to thank the participating patients, their families, all study co-investigators, and research coordinators at the following institutions:

- OHSU Knight Cancer Institute
- Fox Chase Cancer Center
- Royal Marsden Hospital/Institute of Cancer Research
- University of Duisburg-Essen
- Asan Medical Centre
- University Hospitals Leuven
- Erasmus MC Cancer Institute
- Vall d' Hebron Institute of Oncology
- Centre Leon Berard
- Institut Gustave Roussy
- Memorial Sloan Kettering Cancer Center
- Maria Sklodowska-Curie Institute – Oncology Center
- University of Miami Sylvester Comprehensive Cancer Center
- MD Anderson Cancer Center
- Sarcoma Oncology Centre
- Dana-Farber Cancer Institute

Editorial and medical writing support were provided by Lauren Fink, PhD, of Cello Health Communications, and were funded by Blueprint Medicines.


blueprint MEDICINES
Avapritinib precision therapy in advanced GIST
NAVIGATOR Study Update
CTOS 2018 Annual Meeting
November 15, 2018

Conference call participants

Jeff Albers
Chief Executive Officer, Blueprint Medicines

Ben Wolf, MD, PhD
SVP Clinical Development, Blueprint Medicines

Michael Heinrich, MD
Professor of Medicine, Oregon Health and Sciences University

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 development of avapritinib, BLU-554, BLU-667 and BLU-782 and the ability of Blueprint Medicines Corporation (the "Company") to implement those clinical development plans, including plans and timelines for initiating the Phase 2 PIONEER trial, initiating the Phase 3 COMPASS-2L trial and completing enrollment in the Phase 3 VOYAGER trial; the potential benefits of the Company's current and future drug candidates in treating patients, including the potential benefits of avapritinib in treating patients with GIST; plans and timelines for regulatory submissions, filings or discussions, including plans and timelines for submitting a new drug application to the U.S. Food and Drug Administration (the "FDA") for avapritinib for the treatment of PDGFRA-driven GIST and fourth-line GIST; 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 the Company's drug candidates, including avapritinib, BLU-554, BLU-667 and BLU-782; the Company's advancement of multiple early-stage efforts; the Company's ability to successfully demonstrate the efficacy and safety of its drug candidates; the preclinical and clinical results for the Company's drug candidates, which may not support further development of such drug candidates; actions or decisions of regulatory agencies or authorities, which may affect the initiation, timing and progress of clinical trials; the Company's ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing; the Company's ability to develop and commercialize companion diagnostic tests for its current and future drug candidates, including companion diagnostic tests for avapritinib for PDGFRα D842V-driven gastrointestinal stromal tumors, BLU-554 for FGFR4-driven hepatocellular carcinoma and BLU-667 for RET-driven non-small cell lung cancer; and the success of the Company's 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 under "Risk Factors" in the Company's 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 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.

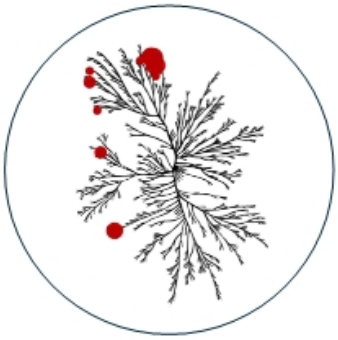
Welcome

Jeff Albers, Chief Executive Officer

Precision therapies for people with cancer and rare diseases

A NEW WAY OF LOOKING AT KINASE MEDICINES

SELECTIVE

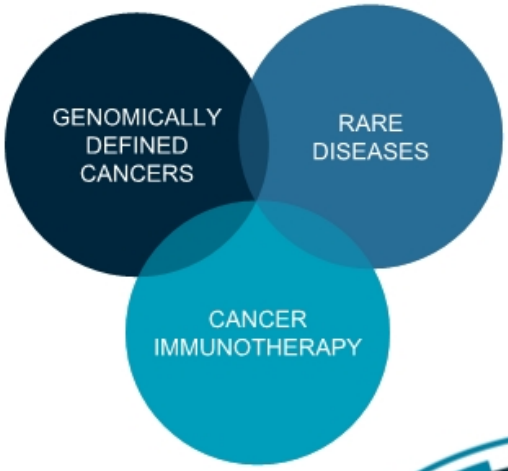


AVAPRITINIB

NON-SELECTIVE

SUTENT® (SUNITINIB)

WITH A FOCUS ON CORE AREAS OF EXPERTISE



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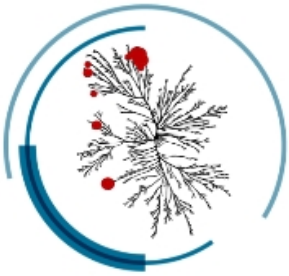
Avapritinib is a potent and highly selective KIT and PDGFRA inhibitor



- Ongoing development in advanced GIST and systemic mastocytosis (SM)
- Breakthrough Therapy Designations for PDGFRα D842V GIST and advanced SM
- Planned NDA in 1H 2019 for PDGFRA-driven and ≥4L GIST
- Blueprint Medicines retains global commercial rights, excluding Greater China*
  - ~30,000 patients across relevant GIST and SM populations in US, EU5 and Japan**

	Advanced GIST Development Program		Systemic Mastocytosis Development Program		
Clinical trial	NAVIGATOR	VOYAGER	EXPLORER	PATHFINDER	PIONEER
Populations	• PDGFRα D842V • 2L • 3L • 4L	• 3L • 4L	• Advanced SM	• Advanced SM	• Indolent SM • Smoldering SM

*CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib in Mainland China, Hong Kong, Macau and Taiwan.
**Represents estimated number of patients with PDGFRA-driven GIST; 2L, 3L, 4L KIT-driven GIST; and advanced, smoldering and indolent SM.
2L, second line; 3L, third line; 4L, fourth line; GIST, gastrointestinal stromal tumors, NDA, new drug application.
Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com) (CSTI). The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content.

Avapritinib is Highly Active and Well-tolerated in Patients With Advanced GIST Driven by a Diverse Variety of Oncogenic Mutations in KIT and PDGFRA

Michael Heinrich, Margaret von Mehren, Robin L. Jones, Sebastian Bauer, Yoon-Koo Kang, Patrick Schöffski, Ferry Eskens, César Serrano, Philippe A. Cassier, Olivier Mir, William D. Tap, Piotr Rutkowski, Jonathan Trent, Shreyaskumar Patel, Sant P. Chawla, Teresa Zhou, Tamieka Lauz, Oleg Schmidt-Kittler, Khalid K. Mamlouk, Beni B. Wolf, Suzanne George

Connective Tissue Oncology Society 2018 Annual Meeting
Rome, Italy • November 15, 2018

Abstract no: 3027631

Disclosures

- Avapritinib is an investigational agent discovered and currently in development by Blueprint Medicines Corporation (Blueprint Medicines)
- Data are preliminary and based on a cutoff date of October 15, 2018
- Dr. Michael Heinrich is an investigator for Blueprint Medicines' ongoing Phase 1 study in unresectable gastrointestinal stromal tumors
- Dr. Michael Heinrich has the following disclosures:
  - Consultant: Blueprint Medicines, Novartis, Molecular MD, Deciphera
  - Research funding: Blueprint Medicines, Deciphera
  - Stock or stock options: Molecular MD
  - Patents: 4 patents on diagnosis and treatment of PDGFRα-mutant GIST, 1 patent on imatinib treatment of GIST

Avapritinib: a highly selective and potent KIT/PDGFRA inhibitor for GIST

GIST mutation(s)		Medical need by mutation	Avapritinib biochemical IC_{50}[1]
KIT Exon 11 deletion	JM domain	1L imatinib is effective 2L sunitinib/3L regorafenib have low ORR/short PFS	0.6 nM
KIT Exon 11 V560G			1 nM
KIT Exon 11/13	ATP binding site	Approved 2L/3L agents have low ORR/short PFS	11 nM
KIT Exon 11/14			28 nM
KIT Exon 11/17	Activation loop		0.1 nM
PDGFRα D842V		No highly effective therapy in any line	0.24 nM

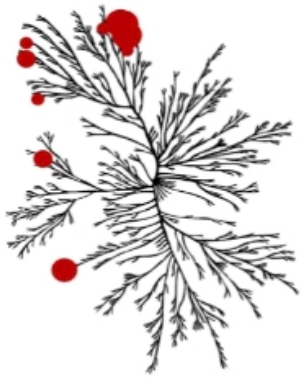
Ongoing clinical trials

NAVIGATOR GIST

Phase 1 advanced GIST

VOYAGER GIST

Phase 3 trial of avapritinib vs. regorafenib in 3L and 4L GIST



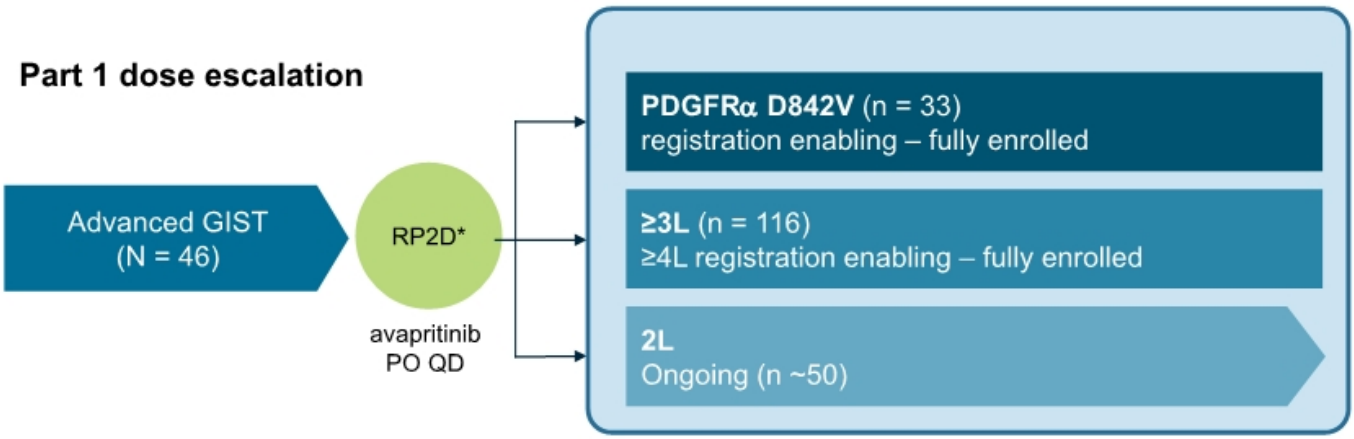
Avapritinib kinome selectivity

KIT, KIT proto-oncogene receptor tyrosine kinase; PDGFRA, platelet-derived growth factor alpha; IC_{50}, concentration causing 50% inhibition; L, line; JM, juxtamembrane; ORR, objective response rate; PFS, progression-free survival.

Kinome illustrations reproduced courtesy of Cell Signaling Technology, Inc. (CSTI) (www.cellsignal.com). Blueprint Medicines is not responsible for the content of the CSTI site.

[1]Evans E, et al. Sci Transl Med. 2017;9(414). pii: eaao1690.

NAVIGATOR Phase 1 study design



KEY OBJECTIVES

- Determine MTD/RP2D, safety, PK and clinical activity by line of therapy and mutational status
- ORR/DOR per central radiology assessment (mRECIST 1.1) for planned NDA and MAA regulatory filings

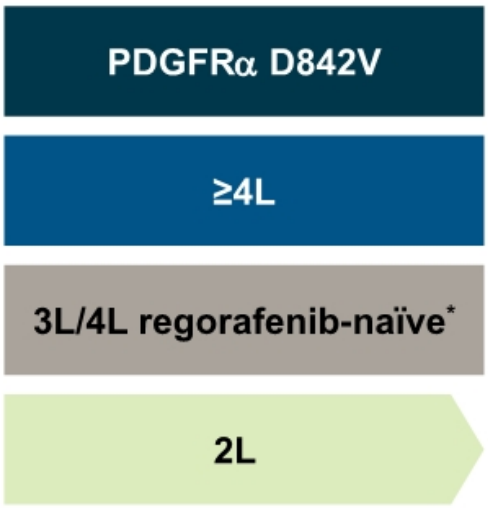
RP2D, recommended Phase 2 dose; PO, orally; QD, once daily; MTD, maximum tolerated dose; PK, pharmacokinetics; DOR, duration of response; mRECIST, modified Response Evaluation Criteria in Solid Tumors; NDA, New Drug Application; MAA, Marketing Authorization Application.
*MTD 400 mg; RP2D 300 mg.

Demography and baseline characteristics

Parameter	All patients (N = 231)	
Age (years), median (range)	62 (25, 90)	
GIST mutational subtype, % (n)		
KIT	72% (167)	
PDGFRα D842V	24% (56)	
PDGFRα non-D842V	4% (8)	
Metastatic disease, % (n)	89% (205)	
Largest target lesion size, % (n)		
≤5 cm	34% (79)	
>5–≤10 cm	40% (93)	
>10 cm	20% (47)	
Pending	5% (12)	
No. prior kinase inhibitors, % (n)	PDGFRα	KIT
Median (range)	1 (0-6)	4 (1-11)
0	17% (11)	0
1	37% (24)	19% (31)
2	19% (12)	8% (14)
3	11% (7)	20% (34)
4	8% (5)	23% (38)
≥5	8% (5)	30% (50)

*Similar to Phase 3 trial population (VOYAGER).
Data are preliminary and based on a cutoff date of October 15, 2018.

Efficacy populations



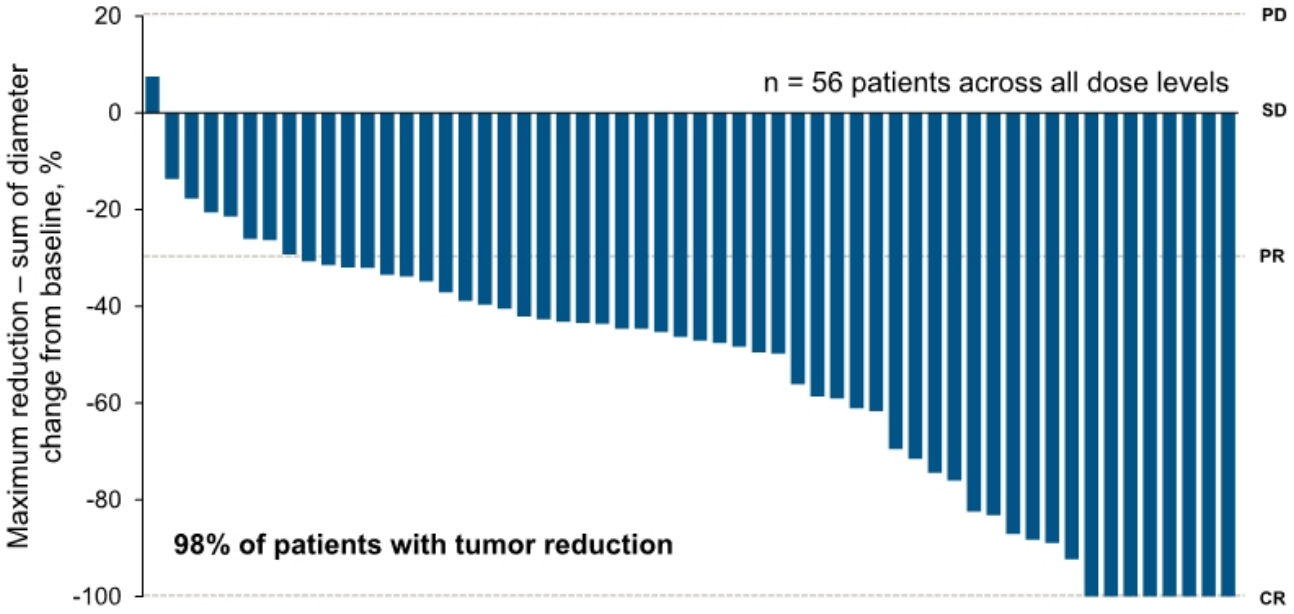
Adverse events ≥20%

Safety population; all doses (N = 231)					
AE, % (n)	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4
Nausea	61% (142)	46% (106)	13% (30)	3% (6)	0
Fatigue	55% (127)	21% (48)	28% (64)	6% (15)	0
Anemia	46% (107)	5% (11)	15% (35)	25% (58)	1% (3)
Periorbital edema	40% (93)	34% (79)	6% (13)	<1% (1)	0
Diarrhea	39% (90)	22% (50)	13% (30)	4% (10)	0
Vomiting	38% (88)	30% (69)	6% (14)	2% (5)	0
Decreased appetite	35% (82)	23% (54)	9% (20)	3% (8)	0
Peripheral edema	33% (77)	23% (53)	10% (22)	<1% (2)	0
Increased lacrimation	31% (72)	28% (64)	3% (8)	0	0
Memory impairment*	26% (60)	19% (45)	6% (15)	0	0
Constipation	23% (53)	14% (32)	8% (18)	<1% (2)	<1% (1)
Face edema	23% (53)	19% (43)	4% (9)	<1% (1)	0
Hair color changes	21% (49)	20% (46)	<1% (2)	<1% (1)	0
Dizziness	20% (47)	16% (38)	3% (8)	<1% (1)	0

AE, adverse event.
*The most commonly reported cognitive AE

- Most AEs are grade 1 or 2
- No treatment-related grade 5 AEs
- 8.7% (20) of patients discontinued due to related AEs
- Grade 3-4 treatment-related AEs ≥2%: anemia, fatigue, hypophosphatemia, increased bilirubin, decreased white blood count/neutropenia, and diarrhea

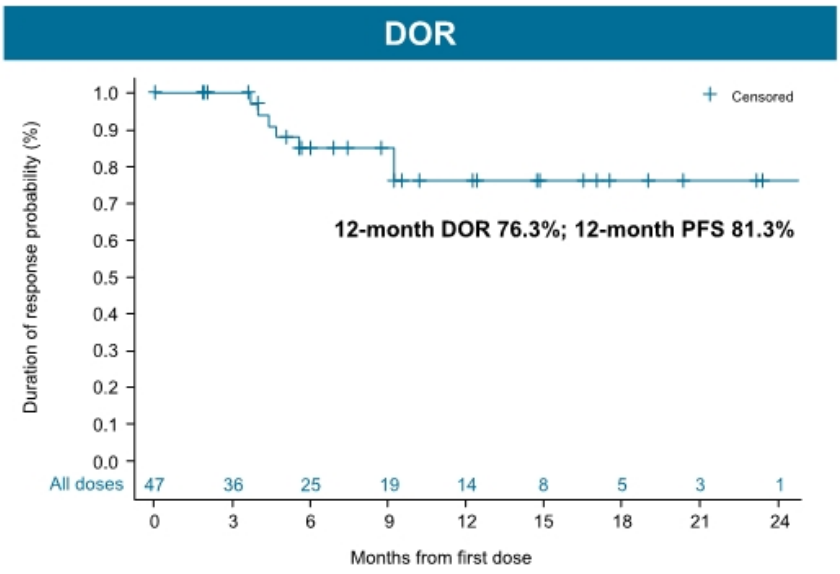
Best response by central radiology in PDGFRα D842V GIST



PD, progressive disease; SD, stable disease; PR, partial response; CR, complete response.

ORR and DOR by central radiology in PDGFRα D842V GIST

Best response* n = 56	mRECIST 1.1 % (n) [95% CI]
ORR	84% (47) [71.7-92.47]
CR/PR*	9% (5)/75% (42)
SD	16% (9)
CBR†	96% (54) [87.7-99.6]



CI, confidence interval; CBR, clinical benefit rate.
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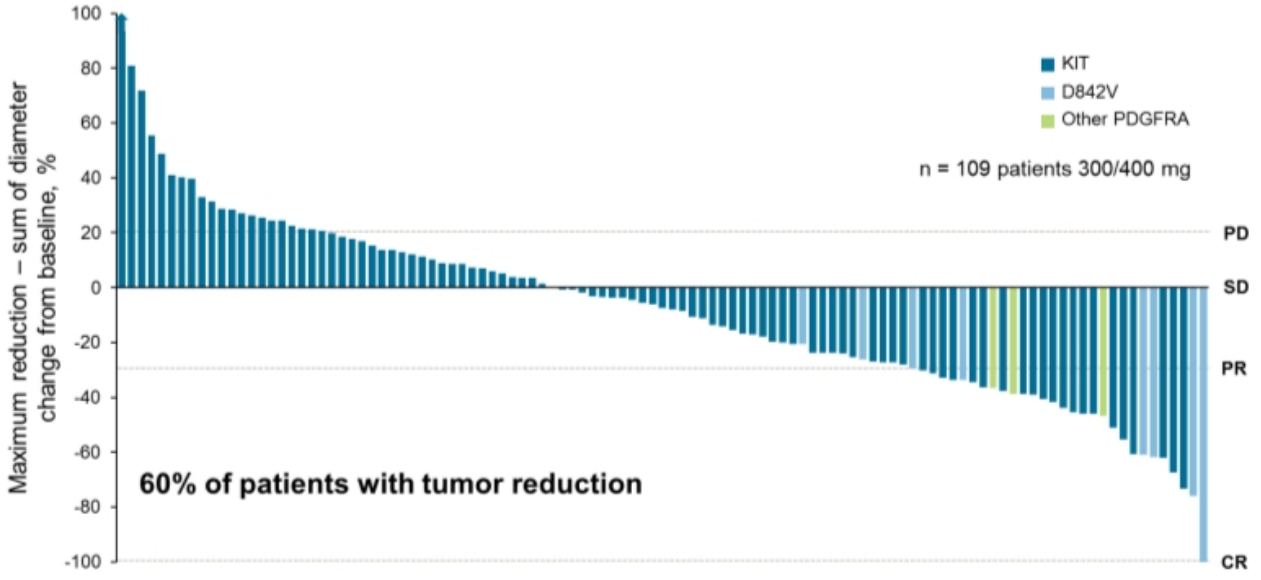
† PR + SD lasting ≥4 months.

Best response by central radiology in ≥4L GIST



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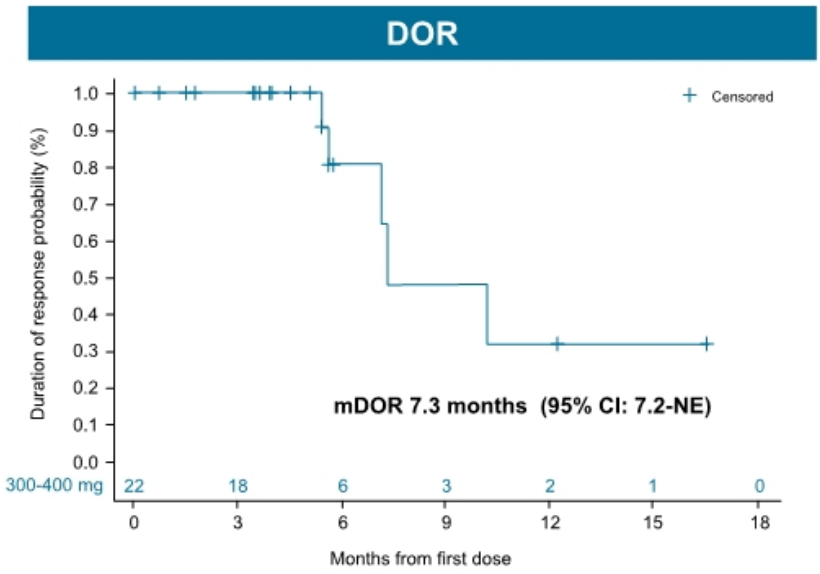

mDOR, median duration of response; NE, not estimatable

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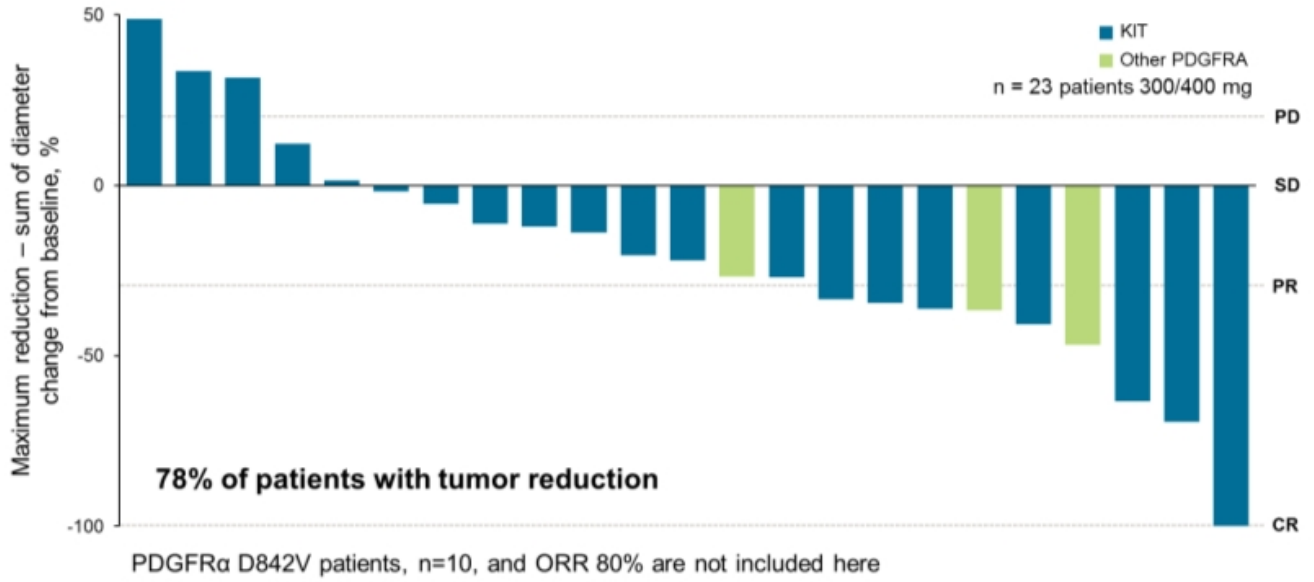
Best response by central radiology in 3L/4L regorafenib-naïve GIST*



*Similar to Phase 3 trial population (VOYAGER), except that PDGFRα D842V patients (ORR 80%) are not included here.

ORR and DOR by central radiology in 3L/4L regorafenib-naïve GIST

Non-D842V patients best response* n = 23	mRECIST 1.1 % (n) [95% CI]
ORR	26% (6) [10.0-48.4]
CR/PR	0% (0)/26% (6)
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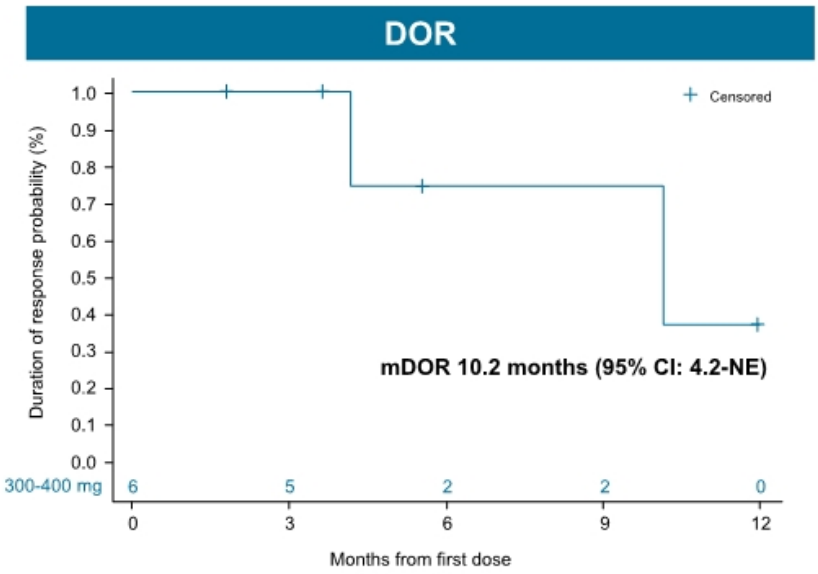

*All responses are confirmed. Patients who have had ≥1 post-baseline radiographic assessment. Response evaluable includes 300 mg and 400 mg.
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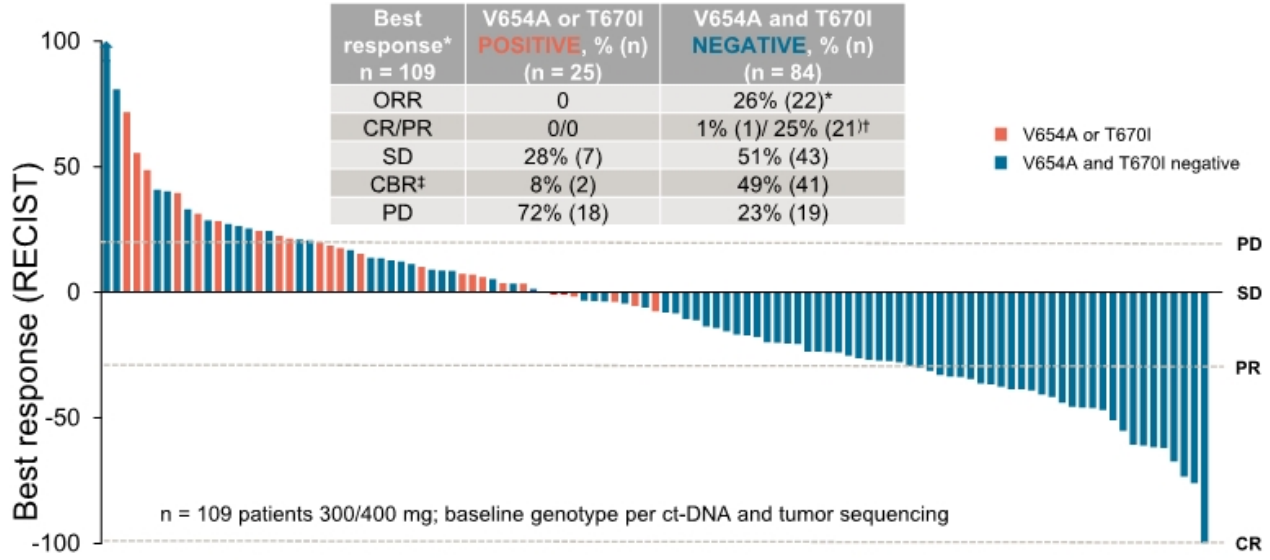
Best response by mutational profile in ≥4L GIST

Best response* n = 109	V654A or T670I POSITIVE, % (n) (n = 25)	V654A and T670I NEGATIVE, % (n) (n = 84)
ORR	0	26% (22)*
CR/PR	0/0	1% (1)/ 25% (21)†
SD	28% (7)	51% (43)
CBR‡	8% (2)	49% (41)
PD	72% (18)	23% (19)



ct-DNA, circulating tumor DNA.

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‡PR + SD lasting ≥4 months

Avapritinib has important clinical activity in advanced GIST

	PDGFRα D842V n = 56	≥4L all patients n = 109	3L/4L regorafenib-naïve non-D842V n = 23	2L non-D842V n = 20
ORR (central radiology), % (n) [95% CI]	84% (47) [72-92]	20% (22) [13.1-29.0]	26% (6) [10.2-48.4]	25% (5) [9-49]
mDOR (central radiology), months [95% CI]	NE [NE, NE]	7.3 [7.2-NE]	10.2 [4.2-NE]	NR
CBR (central radiology), % (n) [95% CI]	96% (54) [88-100]	40% (44) [31.1-50.2]	70% (16) [47.1-86.8]	NR
mPFS (central radiology), months [95% CI]	NE [NE, NE]	3.7 [3.5-5.6]	8.6 [5.6-14.7]	NR
mPFS (investigator), months [95% CI]	22.8 [20.8-28.4]	5.5 [3.8-6.8]	10.2 [5.7-NE]	NR
Benchmarks	**PDGFRα D842V** Approved agents: ORR ~0% mPFS ~3 mo mOS ~15 mo	**4L** imatinib re-treatment: ORR ~0% PFS 1.8 mo	**3L** regorafenib: ORR ~5% PFS 4.8 mo	**2L** sunitinib: ORR ~7% PFS 6 mo

NR, not reported; mPFS, median progression-free survival; mOS, median overall survival.

ORR is not an endpoint for 2L but is early signal readout.

Avapritinib has the potential to change GIST treatment paradigms

- Phase 1 NAVIGATOR study demonstrates favorable tolerability and encouraging clinical activity across lines of therapy
  - Most AEs were grade 1 or 2, with manageable on-target toxicity
  - Important efficacy in PDGFRα D842V GIST and refractory, ≥4L GIST supports regulatory filing
  - Encouraging activity in 3L/4L regorafenib-naïve GIST indicates the potential for a favorable outcome in the ongoing randomized Phase 3 VOYAGER study
  - Mutational profiling analyses and promising 2L data provide strong rationale for genotype-selected 2L study

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- Fox Chase Cancer Center
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- Asan Medical Centre
- University Hospitals Leuven
- Erasmus MC Cancer Institute
- Vall d' Hebron Institute of Oncology
- Centre Leon Berard
- Institut Gustave Roussy
- Memorial Sloan Kettering Cancer Center
- Maria Sklodowska-Curie Institute – Oncology Center
- University of Miami Sylvester Comprehensive Cancer Center
- MD Anderson Cancer Center
- Sarcoma Oncology Centre
- Dana-Farber Cancer Institute

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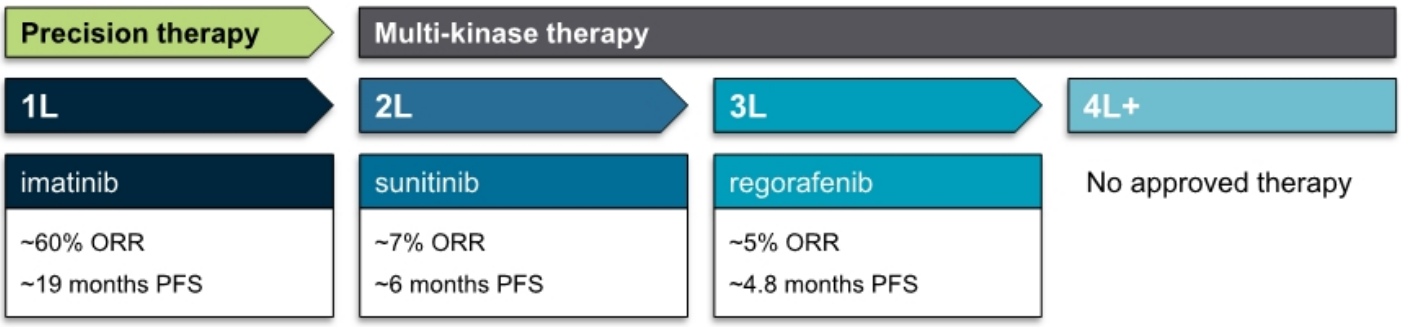
Transforming GIST treatment with precision therapy

Ben Wolf, MD, PhD, SVP Clinical Development

blueprint™ MEDICINES

Current GIST treatment paradigm based on sequential therapy

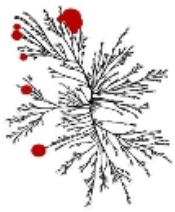


Key Limitations

- No effective therapy for PDGFRA D842V GIST
- No highly effective therapy beyond imatinib for KIT GIST
- Diagnostics are not commonly used to guide patient care

ORR, overall response rate; PFS, progression-free survival.

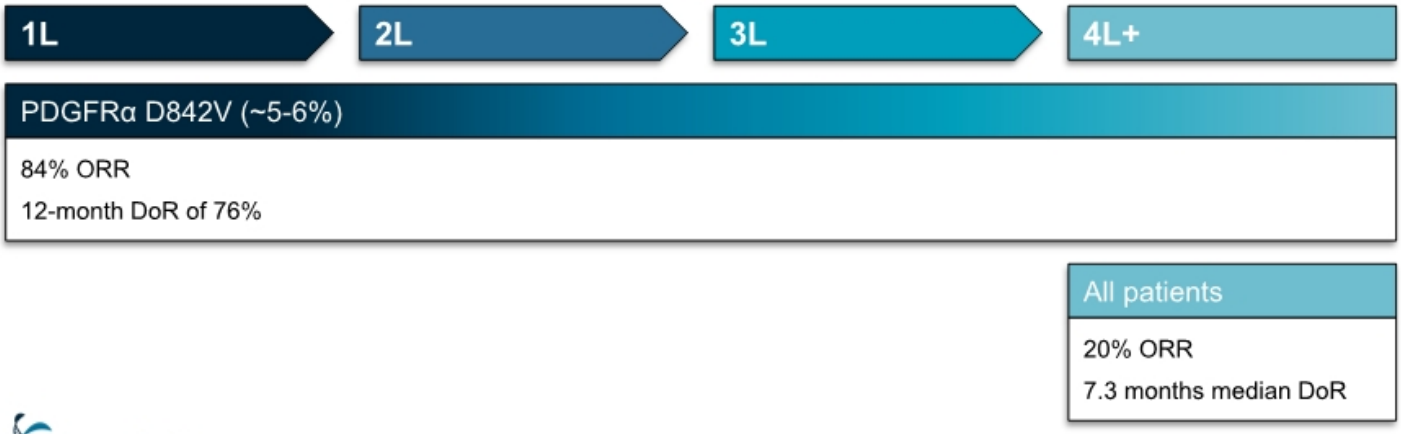
Avapritinib is a potentially transformative selective KIT/PDGFRA inhibitor

	Precision therapies	Multi-kinase therapies	
Approved	 imatinib	 sunitinib	 regorafenib
Investigational	 avapritinib	 DCC-2618	

Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com) (CSTI).
The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content.
All compounds were screened at 3 uM concentration against a panel of 392 wild type kinase constructs using the KINOME*scan* assay platform at DiscoveRx Corporation. The size of the circle indicates binding potency. The bigger the circle, the more potently the compound binds to the particular kinase.

NAVIGATOR enables proof-of-concept and expedited regulatory submissions

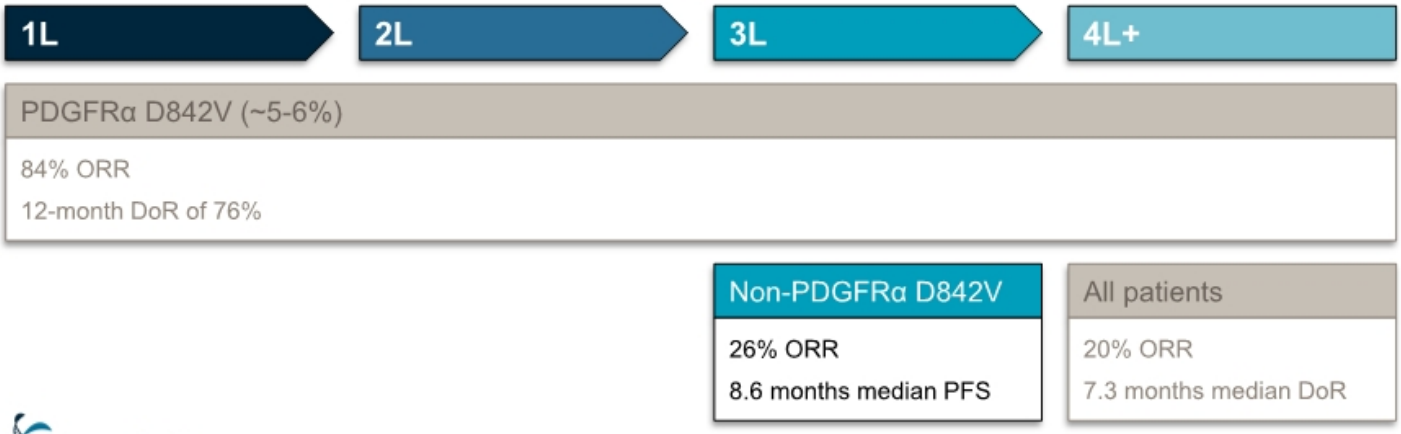
- Anticipated initial NDA submission for PDGFRA-driven and ≥4L GIST
- ORR and DoR per central radiology are primary endpoints for registration



Data previously reported at CTOS Annual Meeting in November 2018. Data cutoff date: October 15, 2018.
DoR, duration of response.

Data show potential for improved ORR and durable benefit in 3L GIST

► Patients with PDGFRα D842V GIST are eligible to participate in VOYAGER study

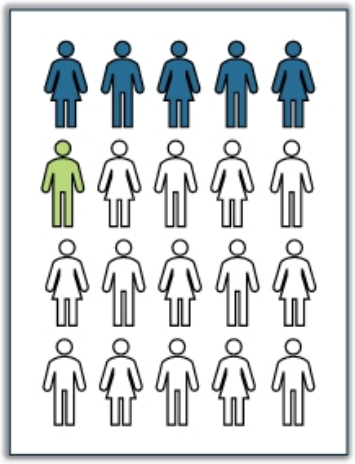


Data previously reported at CTOS Annual Meeting in November 2018. Data cutoff date: October 15, 2018.

Initial data show encouraging activity for avapritinib in 2L GIST

ORR in unselected population	
Non-PDGFRα D842V	25%
PDGFRα D842V	94%

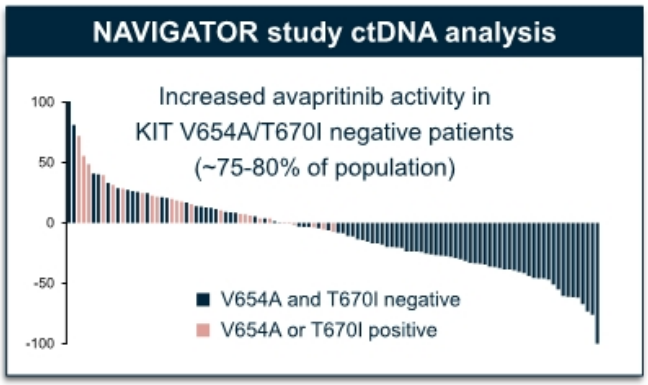
Potential avapritinib activity in unselected population



For illustration purposes only. Actual results will vary.

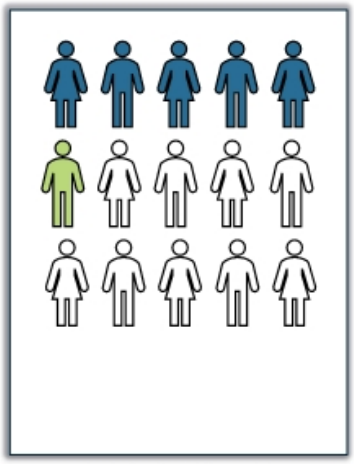
ORR data previously reported at CTOS Annual Meeting in November 2018. Data cutoff date: October 15, 2018.
Estimate 5-6% of primary GIST population has a PDGFRα D842V mutation.

Selection strategy in 2L GIST has the potential to optimize patient outcomes



In 2L GIST, sunitinib has shown activity against KIT V654A and T670I mutations

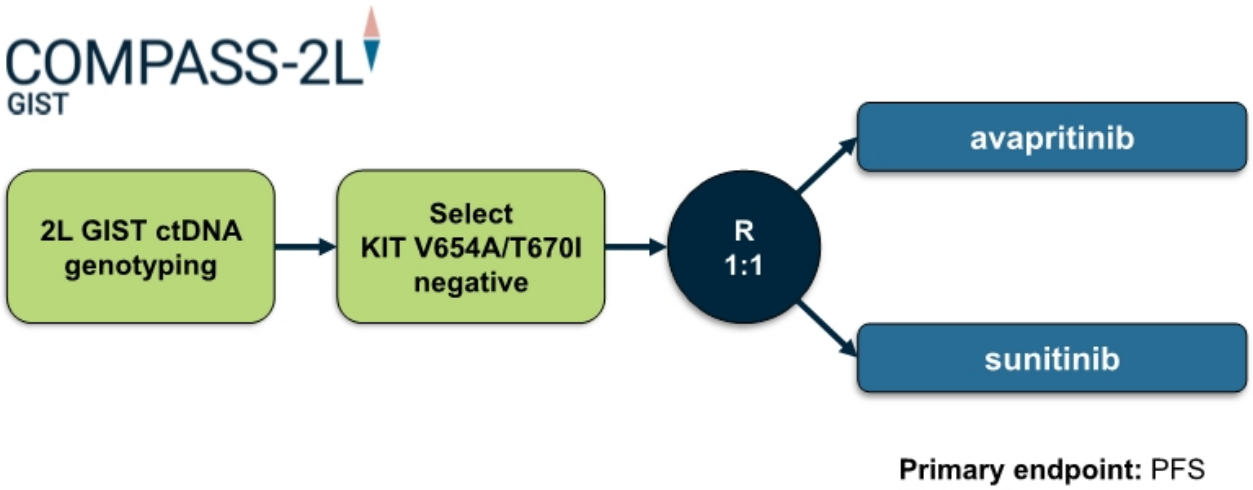
Potential avapritinib activity in selected population (KIT V654A/T670I negative)



For illustration purposes only. Actual results will vary.

Estimated frequency of KIT V654A/T670I mutations based on NAVIGATOR study ctDNA analyses and independent published data.
Reported NAVIGATOR study ctDNA analyses from 4L+ population.
ctDNA data previously reported at CTOS Annual Meeting in November 2018. Data cutoff date: October 15, 2018.

Plan to initiate registration-enabling Phase 3 COMPASS-2L study in 2H 2019



Primary endpoint: PFS

R, randomized

Advancing development of avapritinib across all lines of GIST treatment

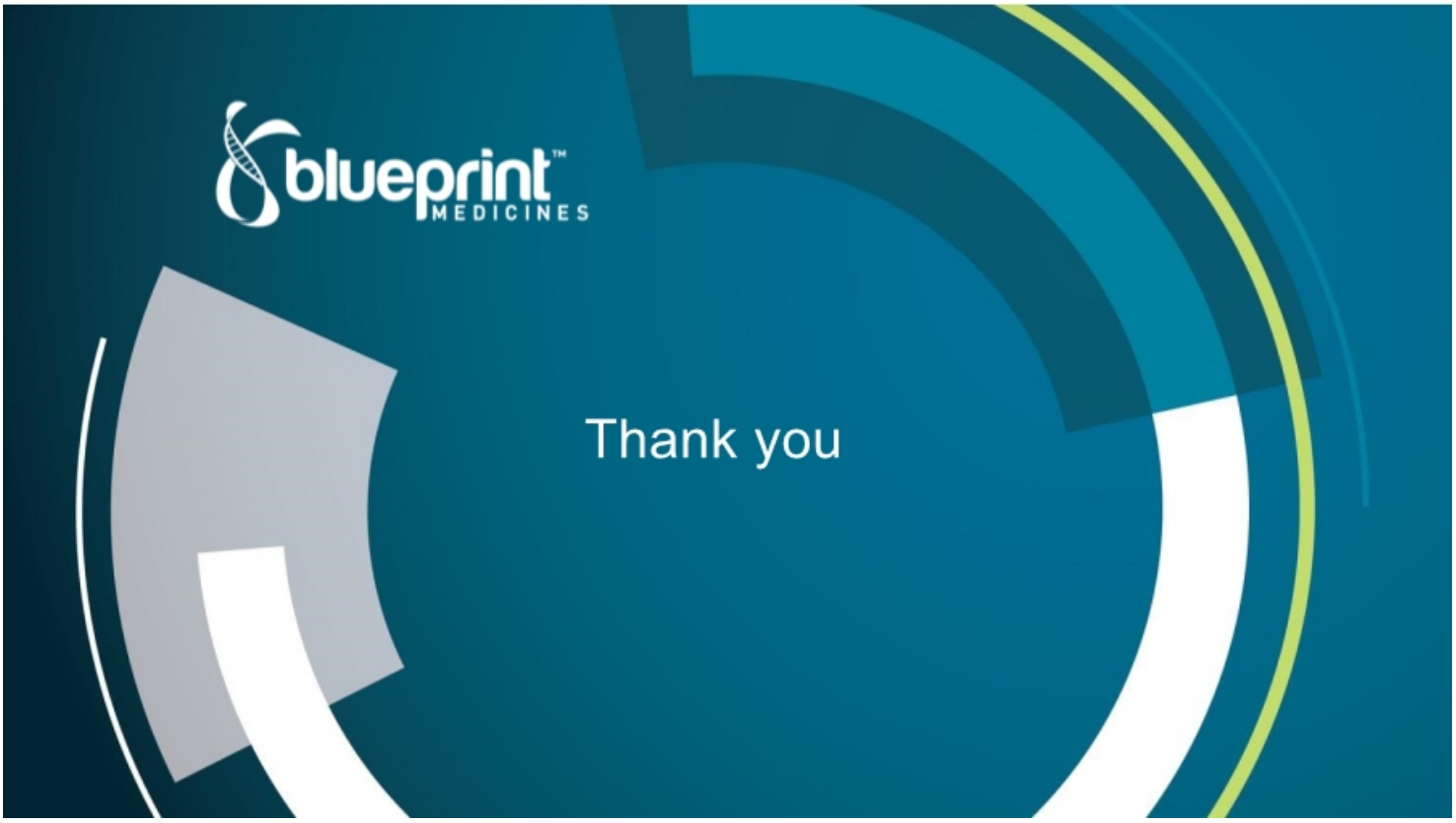
PDGFRα exon 18 ORR 84%; 12 mo DoR 76%	**Ph 1 NAVIGATOR Study** Plan to submit NDA in 1H 2019
≥4L ORR 20.2%; mDoR 7.3 months	**Ph 1 NAVIGATOR Study** Plan to submit NDA in 1H 2019
3L/4L regorafenib-naïve Non-D842V initial ORR 26%; mPFS 8.6 mo	**Ph 3 VOYAGER Study** Expect to complete enrollment in 2H 2019
2L Non-D842V initial ORR 25%	**Ph 3 COMPASS-2L Study** Plan to initiate 2L precision medicine trial in 2H 2019

Data previously reported at CTOS Annual Meeting in November 2018.
mDoR, median duration of response.

Realizing our vision: 6 registration-enabling studies expected in 2019

DRUG CANDIDATE (TARGET)	DISCOVERY	PRECLINICAL	PHASE 1-2	PIVOTAL[1]	COMMERCIAL RIGHTS
avapritinib (KIT & PDGFRα)	Phase 1 NAVIGATOR – Advanced PDGFRA-driven and 4L GIST Phase 1 NAVIGATOR – Advanced 3L GIST Phase 1 NAVIGATOR – Advanced 2L GIST Phase 3 VOYAGER – Advanced 3L GIST Phase 3 COMPASS-2L – Advanced 2L GIST (planned 2H 2019) Phase 1 EXPLORER – Advanced SM Phase 2 PATHFINDER – Advanced SM Phase 2 PIONEER – Indolent and smoldering SM (planned by end of 2018)				*
BLU-554 (FGFR4)	Phase 1 – Advanced hepatocellular carcinoma				
BLU-667 (RET)	Phase 1 ARROW – Advanced NSCLC, thyroid and other cancers[2]				
BLU-782 (ALK2)	Fibrodysplasia ossificans progressiva				
3 undisclosed kinase targets					
Immunokinase targets	Up to 5 cancer immunotherapy programs; development stage undisclosed				Roche **

[1] Potential for study to be registration-enabling. NAVIGATOR trial also has potential to be registration-enabling for fourth-line GIST. [2] ARROW trial includes a basket cohort that consists of other advanced solid tumors with RET alterations.
* CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, BLU-554 and BLU-667 in Mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains all rights in the rest of the world.
** 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.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Thank you