Avapritinib update for the GIST patient and caregiver community

Stephen Miller, PhD
Vice President, Translational Medicine
Blueprint Medicines

LIFE FEST

JULY 14, 2018

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; plans and timelines for reporting data for the Company’s current or future clinical trials; the potential benefits of the Company’s current and future drug candidates in treating patients; plans and timelines for regulatory submissions, filings or discussions, including a first New Drug Application for avapritinib for the treatment of PDGFRα D842V-driven gastrointestinal stromal tumors (“GIST”); plans and timelines for the development and commercialization of companion diagnostics for the Company’s current or future drug candidates; plans and timelines for current or future discovery programs; plans and timelines for any current or future collaborations with strategic partners; 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 BLU-554 for FGFR4-driven hepatocellular carcinoma, avapritinib for PDGFRα D842V-driven GIST 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 March 31, 2018, as filed with the Securities and Exchange Commission (“SEC”) on May 2, 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.

Introduction to Blueprint Medicines

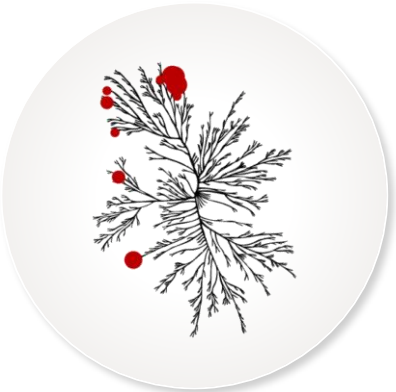
Blueprint Medicines at the Massachusetts State House on Rare Disease Day

- Based in Cambridge, Mass.
- ~150+ employees strong
- Founded by the team who discovered and developed Gleevec® (imatinib)
- Developing targeted kinase medicines for patients with genomically defined diseases
- Culture of urgency to develop medicines for underserved patients

A new way of looking at kinase medicines

Highly selective kinase medicines offer potential for
improved potency, less off-target activity and increased probability of clinical success

SELECTIVE



AVAPRITINIB

NON-SELECTIVE

SUTENT® (SUNITINIB)

RYDAPT® (MIDOSTAURIN)

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.

Realizing our vision for Blueprint Medicines

DRUG CANDIDATE (TARGET)	DISCOVERY	PRECLINICAL	PHASE 1-2	PIVOTAL	COMMERCIAL RIGHTS
avapritinib (KIT & PDGFRα)	Phase 1 NAVIGATOR – Advanced PDGFRA-driven GIST Phase 1 NAVIGATOR – Advanced 3L+ (KIT-driven) GIST Phase 1 NAVIGATOR – 2L (KIT-driven) GIST Phase 3 VOYAGER – Advanced 3L GIST Phase 1 EXPLORER – Advanced systemic mastocytosis (SM) Phase 2 PATHFINDER – Advanced systemic mastocytosis (planned mid 2018) Phase 2 PIONEER – Indolent and smoldering systemic mastocytosis (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[1]				
BLU-782 (ALK2)	Fibrodysplasia ossificans progressiva				
3 undisclosed kinase targets					
Immunokinase targets	Up to 5 cancer immunotherapy programs; development stage undisclosed				 **

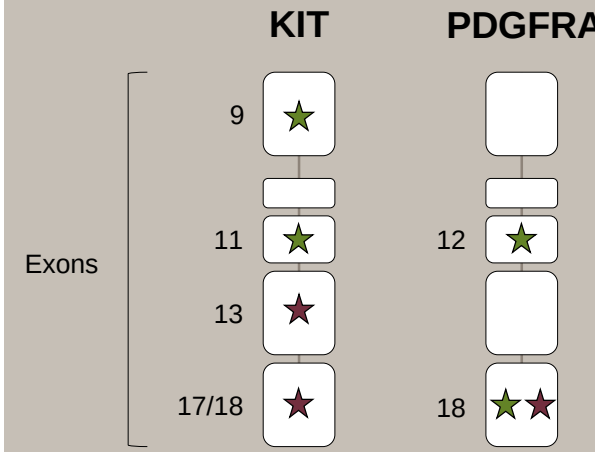
2L, second-line; 3L, third-line; GIST, gastrointestinal stromal tumors; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis

[1] 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.

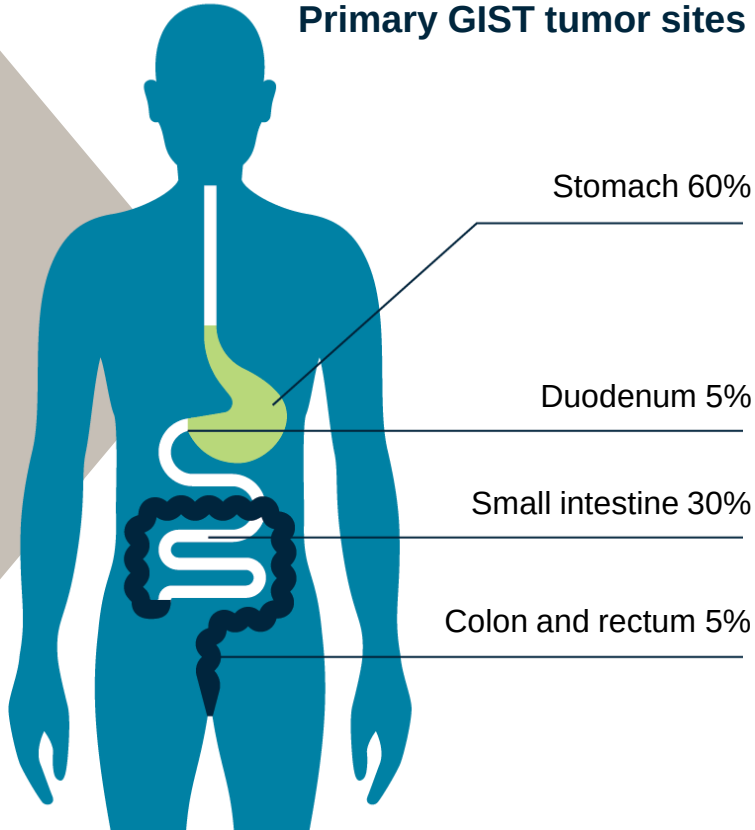
Most GIST cases are caused by mutations in KIT or PDGFRA



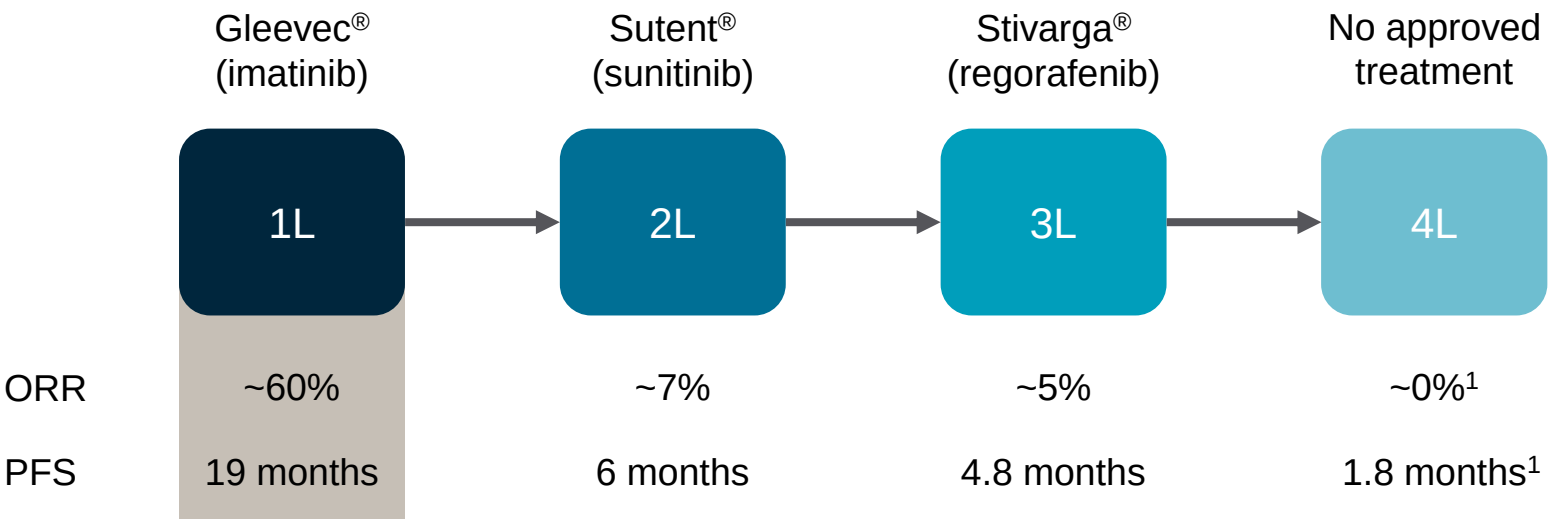
Mutational hotspots

- Primary mutations
- Resistance mutations

- KIT mutations drive about 75-80% of GIST
- PDGFRA mutations drive about 5-10% of GIST



Beyond Gleevec® (imatinib), there are no highly effective therapies for patients with advanced GIST



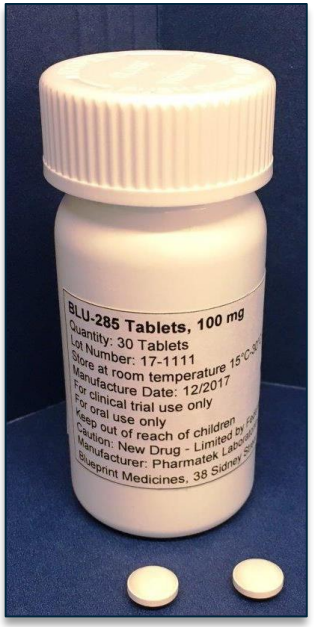
All FDA approved treatments are ineffective against PDGFRα D842V-driven GIST

1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line; ORR, overall response rate; PFS, progression free survival

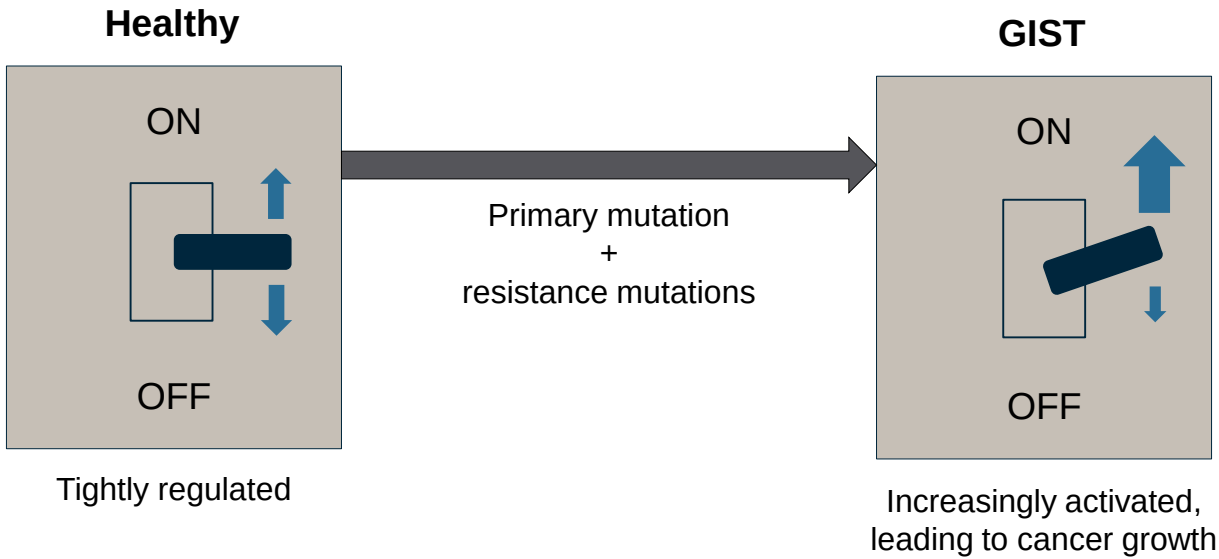
[1] Kang YK, Ryu MH, Yoo C, Ryoo BY, Kim HJ, Lee JJ, et al. Resumption of imatinib to control metastatic or unresectable gastrointestinal stromal tumours after failure of imatinib and sunitinib (RIGHT): a randomised, placebo-controlled, phase 3 trial. Lancet Oncol. 2013;14(12):1175-82.

Avapritinib (formerly known as BLU-285)

- Experimental medicine
- Potent and selective inhibitor of KIT and PDGFRA
- Currently being evaluated in clinical trials for advanced GIST and advanced systemic mastocytosis
- Oral medication taken by mouth once a day
- Granted FDA Breakthrough Therapy Designation for the treatment of PDGFRα D842V-driven GIST



KIT and PDGFRA are increasingly activated in patients with GIST



- Avapritinib is uniquely designed to bind to the active “on” conformation of KIT and PDGFRA
- This design enables potent inhibition of primary and secondary mutants that shift the kinase towards its active conformation
- Current treatments only bind to the inactive “off” conformation

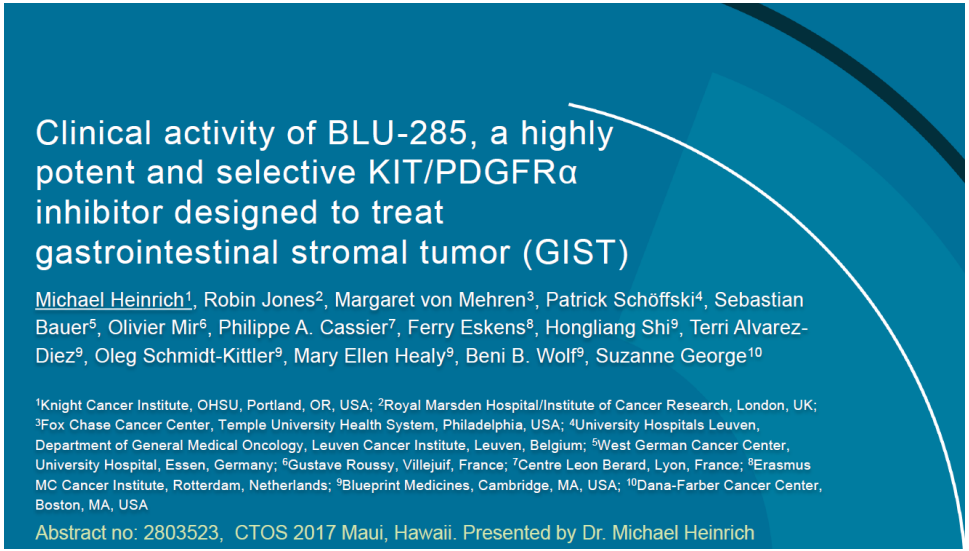
Avapritinib potently inhibits the spectrum of clinically relevant KIT and PDGFRA mutations in advanced GIST

		BLU-285 IC_{50}	Imatinib IC_{50}
KIT Exon 11 deletion	JM domain mutations	0.6 nM	12 nM
KIT Exon 11 V560G		1 nM	87 nM
KIT Exon 11/13	ATP binding site mutations	11 nM	9160 nM
KIT Exon 11/14		28 nM	19650 nM
KIT Exon 17	Activation loop mutations	<2 nM	60–12750 nM
KIT Exon 17 D816V		0.27 nM	8150 nM
PDGFRα Exon 18 D842V		0.24 nM	759 nM

nM, nanomolar

Evans EK et al. Sci Transl Med. 2017 Nov 1;9(414).

Updated data from the Phase 1 NAVIGATOR trial was reported at the CTOS Annual Meeting in November 2017



Clinical activity of BLU-285, a highly potent and selective KIT/PDGFRα inhibitor designed to treat gastrointestinal stromal tumor (GIST)

Michael Heinrich[1], Robin Jones[2], Margaret von Mehren[3], Patrick Schöffski[4], Sebastian Bauer[5], Olivier Mir[6], Philippe A. Cassier[7], Ferry Eskens[8], Hongliang Shi[9], Terri Alvarez-Diez[9], Oleg Schmidt-Kittler[9], Mary Ellen Healy[9], Beni B. Wolf[9], Suzanne George[10]

[1]Knight Cancer Institute, OHSU, Portland, OR, USA; [2]Royal Marsden Hospital/Institute of Cancer Research, London, UK; [3]Fox Chase Cancer Center, Temple University Health System, Philadelphia, USA; [4]University Hospitals Leuven, Department of General Medical Oncology, Leuven Cancer Institute, Leuven, Belgium; [5]West German Cancer Center, University Hospital, Essen, Germany; [6]Gustave Roussy, Villejuif, France; [7]Centre Leon Berard, Lyon, France; [8]Erasmus MC Cancer Institute, Rotterdam, Netherlands; [9]Blueprint Medicines, Cambridge, MA, USA; [10]Dana-Farber Cancer Center, Boston, MA, USA

Abstract no: 2803523, CTOS 2017 Maui, Hawaii. Presented by Dr. Michael Heinrich

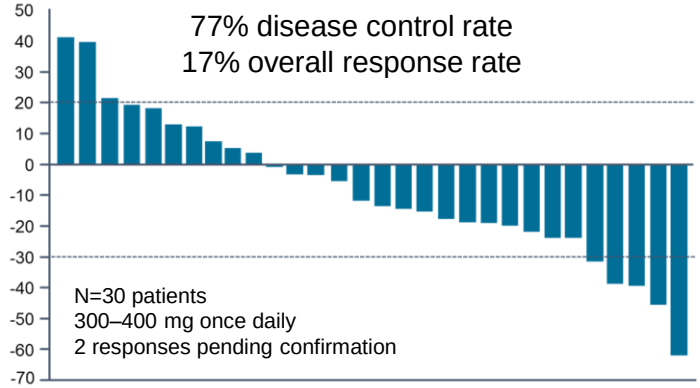
ctos | Bringing together the world's sarcoma specialists

Connective Tissue Oncology Society 2017 Annual Meeting
November 8-11, 2017
Maui, Hawaii

blueprint™ MEDICINES

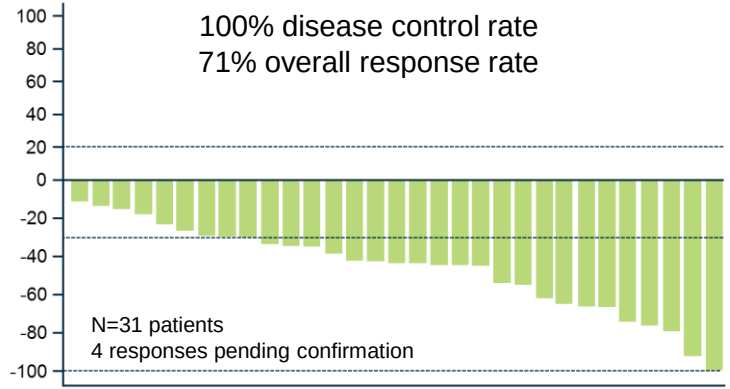
Tumor reduction and prolonged progression free survival observed in patients with advanced GIST

KIT-driven GIST (median 4 prior therapies)



- Median progression free survival of 11.5 months

PDGFRα D842-driven GIST



- Median progression free survival not reached
- 78% of patients had not progressed at 12 months

Data previously presented in November 2017 at the CTOS Annual Meeting. Data cutoff: October 11, 2017.

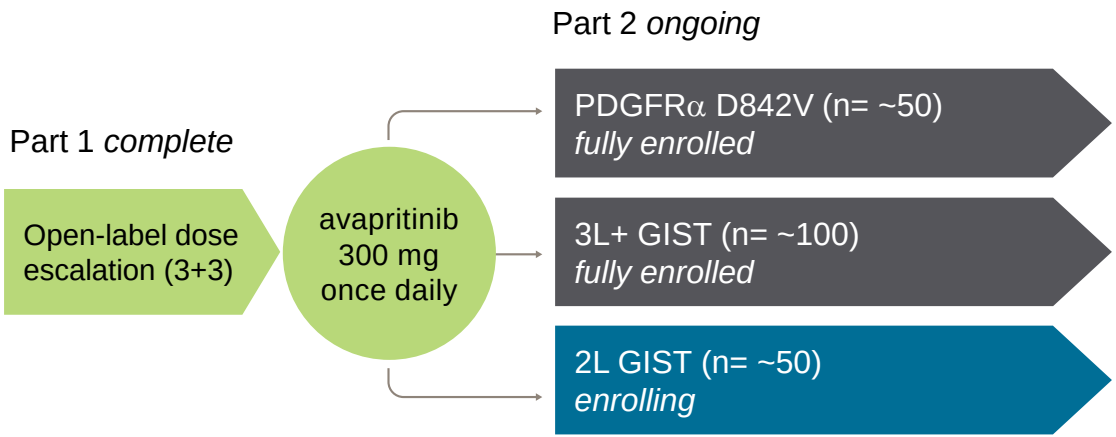
Avapritinib has been generally well tolerated in patients with GIST

- Most adverse events were Grade 1 or 2 (mild or moderate)
- Only 6 patients (5%) discontinued treatment with avapritinib due to adverse events
- Regardless of severity or relationship to treatment with avapritinib, the most common adverse events occurring in 25% or more patients included:
  - Nausea (56%), fatigue (53%), periorbital edema (43%), vomiting (41%), peripheral edema (34%), anemia (31%), diarrhea (31%), increased lacrimation (30%), cognitive effects (30%), decreased appetite (28%)
- Treatment-related ≥Grade 3 (severe) adverse events were reported in 39 patients (34%)

AE, adverse event. Data previously presented in November 2017 at the CTOS Annual Meeting. Data cutoff: October 11, 2017.
Cognitive effects are an aggregated category of individual cognitive events, each of which was observed in fewer than 20% of patients.

Phase 1 NAVIGATOR clinical trial now enrolling patients with 2L GIST

NAVIGATOR GIST



Key endpoints: overall response rate, duration of response, safety

Design

- Open-label, Phase 1 clinical trial
- All enrolled patients receive avapritinib

Eligibility

- Aged 18 years or older
- Metastatic and/or unresectable GIST
- Have received Gleevec® (imatinib) or are intolerant to imatinib

More Information

- Website: www.NavigatorStudy.com
- Email: studydirector@blueprintmedicines.com

blueprint™ MEDICINES

Phase 1 NAVIGATOR U.S. trial sites now enrolling patients with 2L GIST

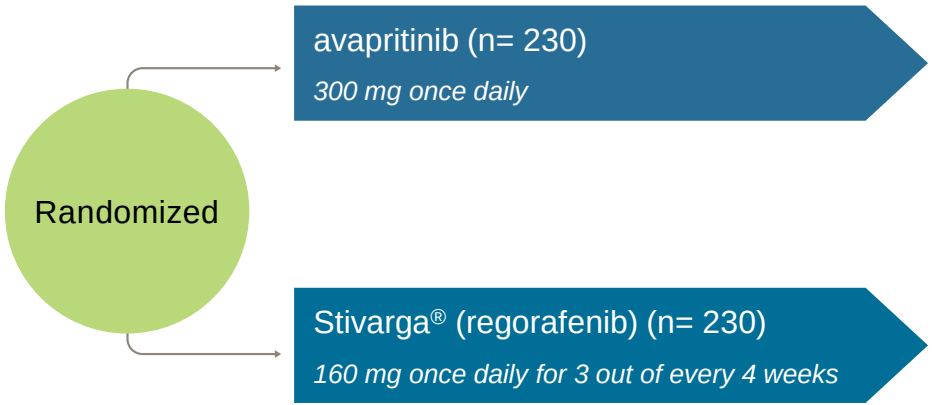
★ Active

Additional trial sites active in Europe, United Kingdom, and Asia

A **travel support program** is available to qualifying patients and caregivers and includes reimbursement of eligible local and long-distance travel and lodging

Phase 3 VOYAGER clinical trial now enrolling patients with 3L and 4L GIST

VOYAGER GIST



Primary endpoint: progression free survival

Design

- Open-label, randomized, Phase 3 clinical trial
- Patients randomized to receive either avapritinib or Stivarga® (regorafenib)
- Patients assigned to receive regorafenib may cross over to receive avapritinib following confirmed disease progression

Eligibility

- Aged 18 years or older
- Metastatic and/or unresectable GIST
- Have received Gleevec® (imatinib) and 1 or 2 other tyrosine kinase inhibitors

More Information

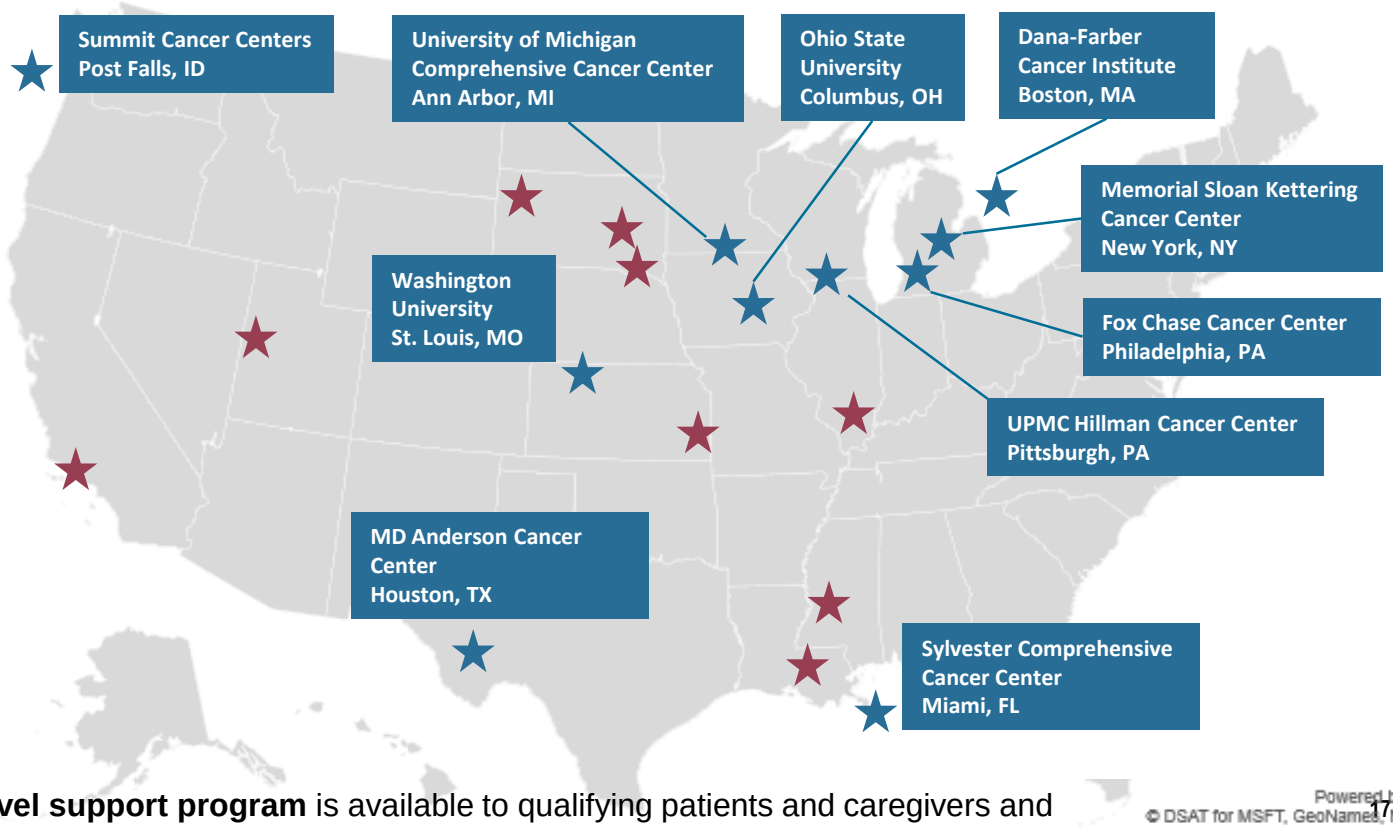
- Website: www.VoyagerTrial.com
- Email: studydirector@blueprintmedicines.com

blueprint MEDICINES

Phase 3 VOYAGER U.S. trial sites now enrolling patients with 3L and 4L GIST

★ Active
★ Planned

Additional trial sites active or planned in Canada, Europe, United Kingdom, Australia and Asia



A **travel support program** is available to qualifying patients and caregivers and includes reimbursement of eligible local and long-distance travel and lodging

Summary of key avapritinib updates

- Granted FDA Breakthrough Therapy Designation for the treatment of PDGFRα D842V-driven GIST
- Completed enrollment of cohorts for patients with PDGFRα D842V-driven GIST and 3L+ (KIT-driven GIST) in Phase 1 NAVIGATOR clinical trial
  - Additional cohort for patients with 2L GIST is actively enrolling
- Initiated Phase 3 VOYAGER clinical trial for patients with 3L and 4L GIST
- Plan to report updated data from the NAVIGATOR trial in the second half of 2018
- Plan to submit a New Drug Application for the approval of avapritinib for the treatment of patients with PDGFRα D842V-driven GIST in the first half of 2019

Questions and Answers

Clinical trial inquiries:

studydirector@blueprintmedicines.com