Avapritinib update for the GIST patient and caregiver community

Jim Baker
Vice President, Corporate Affairs
Blueprint Medicines

LIFE RAFT GROUP CANADA
HALIFAX GIST DAY OF LEARNING
MAY 26, 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; the potential benefits of the Company’s current and future drug candidates in treating patients; plans and timelines for regulatory submissions, filings or discussions; plans and timelines for the development and commercialization of companion diagnostics for the Company’s current or future drug candidates; plans and timelines for current or future discovery programs; plans and timelines for any current or future collaborations with strategic partners; expectations regarding the Company’s existing cash, cash equivalents and investments or the future financial performance of the Company; expectations regarding potential milestones; and the Company’s strategy, business plans and focus. The Company has based these forward-looking statements on management’s current expectations, assumptions, estimates and projections. While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks, uncertainties and other important factors, many of which are beyond the Company’s control and may cause actual results, performance or achievements to differ materially from those expressed or implied by any forward-looking statements. These risks and uncertainties include, without limitation, risks and uncertainties related to the delay of any current or planned clinical trials or the development of 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 HCC, 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 or future collaborations, including its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc.

These and other risks and uncertainties are described in greater detail under “Risk Factors” in the Company’s Quarterly Report on Form 10-Q for the quarter ended 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.

Medical disclaimer

- Today’s presentation is for educational purposes only
- Information in this presentation is not intended to replace the advice of a medical professional and does not constitute medical advice
- If you have questions about your care, please speak with your physician or health care provider

Introduction to Blueprint Medicines

Jim Baker - VP, Corporate Affairs

Blueprint Medicines at the Massachusetts State House on Rare Disease Day

- Based in Cambridge, Mass.
- ~160 employees strong
- Founded by the team who discovered and developed Gleevec (imatinib)
- Developing targeted kinase medicines for 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 (FORMERLY BLU-285)

NON-SELECTIVE

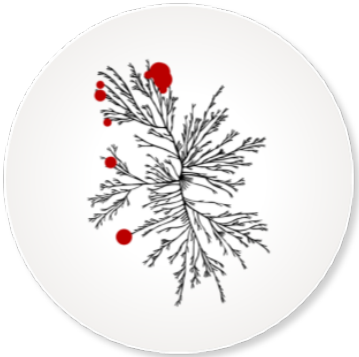
SUTENT® (SUNITINIB)

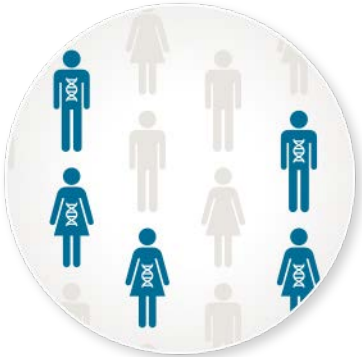
RYDAPT® (MIDOSTAURIN)

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.

Clinical strategy to rapidly bring transformative medicines to patients

GENOMIC DRIVER OF DISEASE ❯ HIGHLY SELECTIVE KINASE MEDICINE ❯ SELECTED PATIENT POPULATION ❯ TARGET OUTCOMES





- Achieve rapid clinical proof-of-concept
- Early go/no-go decisions
- Expedited development & regulatory approval
- Clear commercial value proposition

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 PDGFRα-driven GIST Phase 1 NAVIGATOR – Advanced 3L+ (KIT-driven) GIST Phase 1 NAVIGATOR – 2L (KIT-driven) GIST Phase 3 VOYAGER – Advanced 3L GIST (planned Q2 2018) 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[2]				

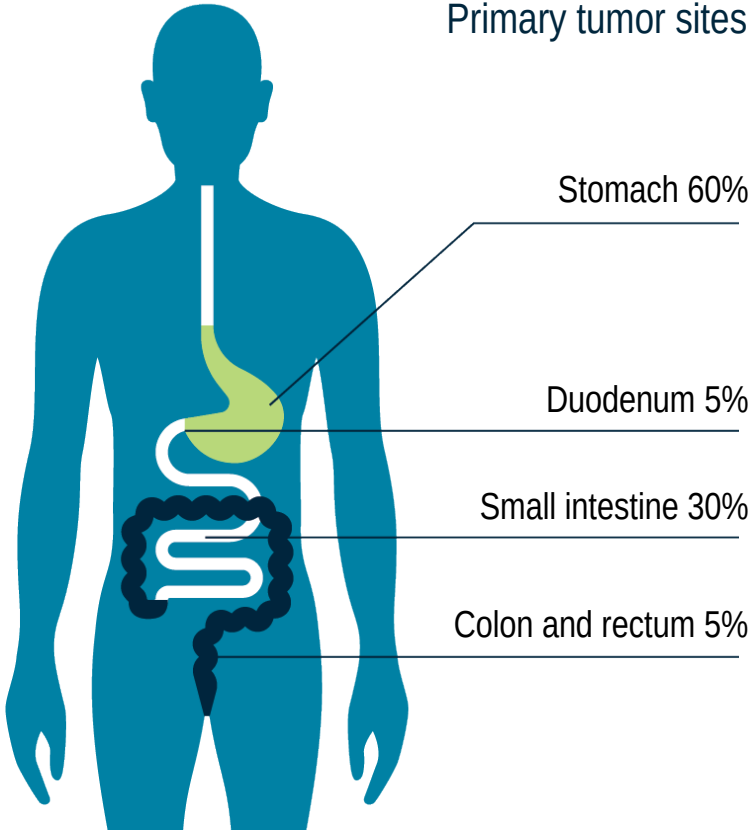
2L, second-line; 3L, third-line

[1] ARROW trial includes a basket cohort that consists of other advanced solid tumors with RET alterations.

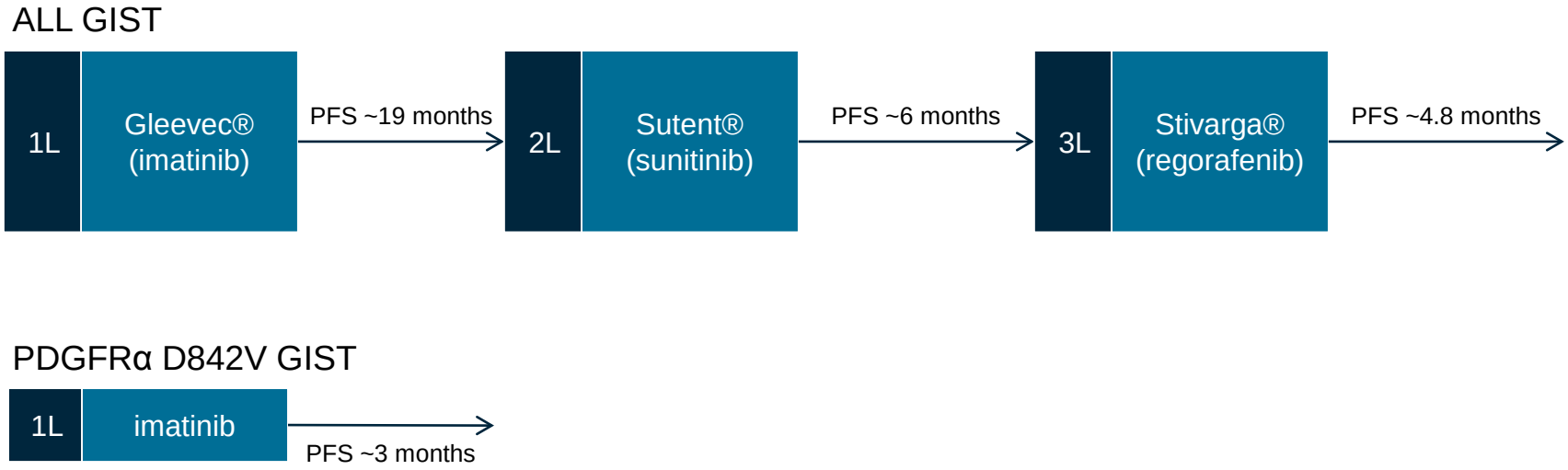
[2] Blueprint Medicines has U.S. commercial rights for up to two programs. Roche has worldwide commercialization rights for up to three programs and ex-U.S. commercialization rights for up to two programs.

Gastrointestinal stromal tumors (GIST): an overview

- Typically presents as stomach or intestinal mass
- Metastases in liver, lining of the abdominal cavity (peritoneum) and other distant sites
- Mutant receptor tyrosine kinases are key disease drivers
  - PDGFRα ~5-10%
  - KIT ~75-80%



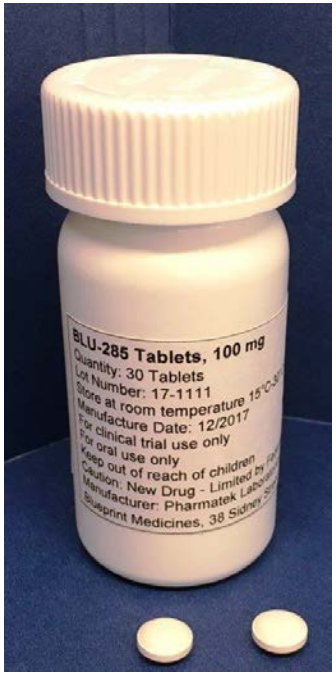
Current FDA approved treatments for GIST



PFS: progression free survival

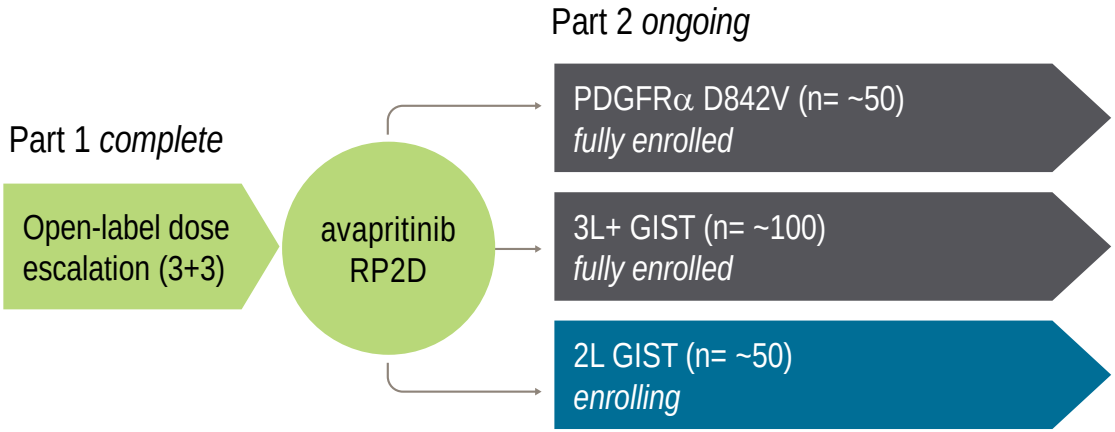
BLU-285 is a potent and selective inhibitor of KIT and PDGFRα

- Investigational new drug
  - Discovered and developed by Blueprint Medicines
  - Undergoing evaluation in clinical trials in patients with advanced GIST and advanced systemic mastocytosis
- Oral medication
  - Supplied in capsules or tablets
  - Taken by mouth once a day
- Designed to selectively inhibit a spectrum of mutations in KIT and PDGFRα kinases thought to underlie GIST



Ongoing Phase 1 NAVIGATOR clinical trial

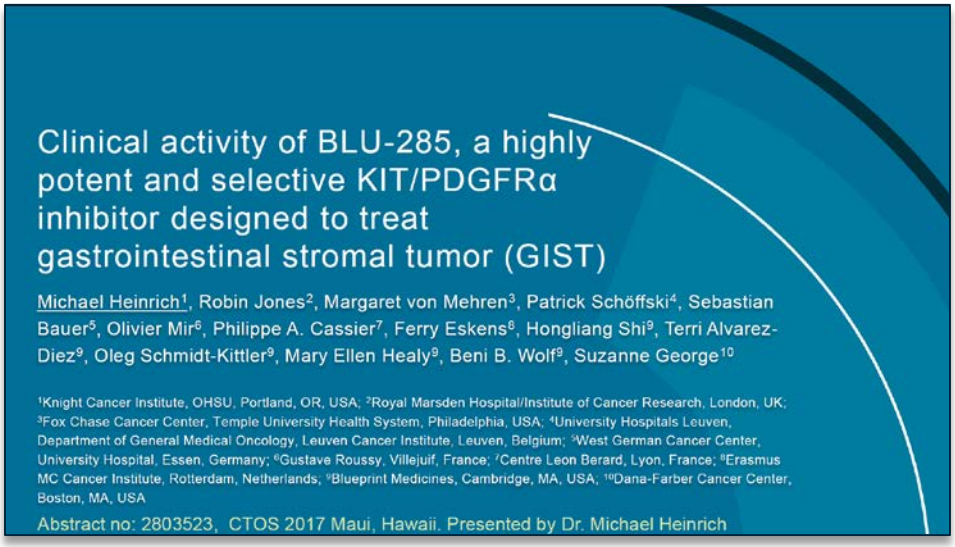
NAVIGATOR GIST



Key Part 2 goals: safety, overall response rate, duration of response

RP2D, recommended part 2 dose

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

Demography and baseline patient characteristics

Parameter	All patients, N=116	
Age (years), median (range)	62 (25–85)	
	n (%)	
GIST subtype*		
KIT mutant	76 (66)	
PDGFRα D842 mutant	37 (32)	
PDGFRα Exon 14 (N659K) mutant	2 (2)	
KIT & PDGFRα WT	1 (1)	
Metastatic disease	107 (92)	
Largest target lesion size (cm)		
≤5	27 (23)	
>5–≤10	42 (36)	
>10	46 (40)	
pending	1 (1)	
No. prior kinase inhibitors	PDGFRα	KIT
Median (range)	1 (0–6)	4 (2–11)
≥3	11 (28)	67 (87)
Prior regorafenib	8 (21)	64 (83)

* Data are preliminary and based on a cut off date of 11 Oct 2017

Treatment emergent adverse events occurring in 20% or more patients

Safety population (all patients) N=116		Severity				
Preferred Term, n (%)	Any AE	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Nausea	65 (56)	41 (35)	17 (15)	7 (6)	0	0
Fatigue	62 (53)	23 (20)	31 (27)	8 (7)	0	0
Periorbital edema	50 (43)	42 (36)	8 (7)	0	0	0
Vomiting	48 (41)	36 (31)	9 (8)	3 (3)	0	0
Edema peripheral	39 (34)	28 (24)	9 (8)	2 (2)	0	0
Anemia	36 (31)	7 (6)	10 (9)	17 (15)	2 (2)	0
Diarrhea	36 (31)	26 (22)	8 (7)	2 (2)	0	0
Cognitive Effects*	35 (30)	20 (17)	10 (9)	4 (3)	1 (1)	0
Lacrimation increased	35 (30)	29 (25)	6 (5)	0	0	0
Decreased appetite	33 (28)	24 (21)	6 (5)	3 (3)	0	0
Dizziness	27 (23)	21 (18)	6 (5)	0	0	0
Constipation	25 (22)	18 (16)	6 (5)	0	1 (1)	0
Hair color changes	25 (22)	24 (21)	0	0	0	0

* Consists of multiple similar adverse events that have been aggregated into a single category. 42% of patients at 400 mg (MTD), 18% of patients at 300 mg (RP2D).

- 39 (34%) patients had grade ≥3 treatment-related adverse events: anemia (9%), fatigue (7%), hypophosphatemia (4%), nausea (4%), cognitive effects (3%)
- 67 patients on treatment; 49 discontinued: progression n=40, adverse events n=6, withdrew consent n=3

In the Phase 1 trial, clinical activity is assessed using two response criteria

Response Evaluation Criteria In Solid Tumors (RECIST)

- Measures tumor size by computerized tomography (CT) or magnetic resonance imaging (MRI)
- Potential to provide the basis for regulatory approval

Choi response criteria for soft tissue sarcomas

- Incorporates changes in both tumor size and density by computerized tomography (CT)
- Used to assist interpretation of clinical response data

RECIST Response Types

Complete Response (CR)

- Disappearance of targeted tumors

Partial Response (PR)

- At least a 30% decrease in tumor size

Progressive Disease (PD)

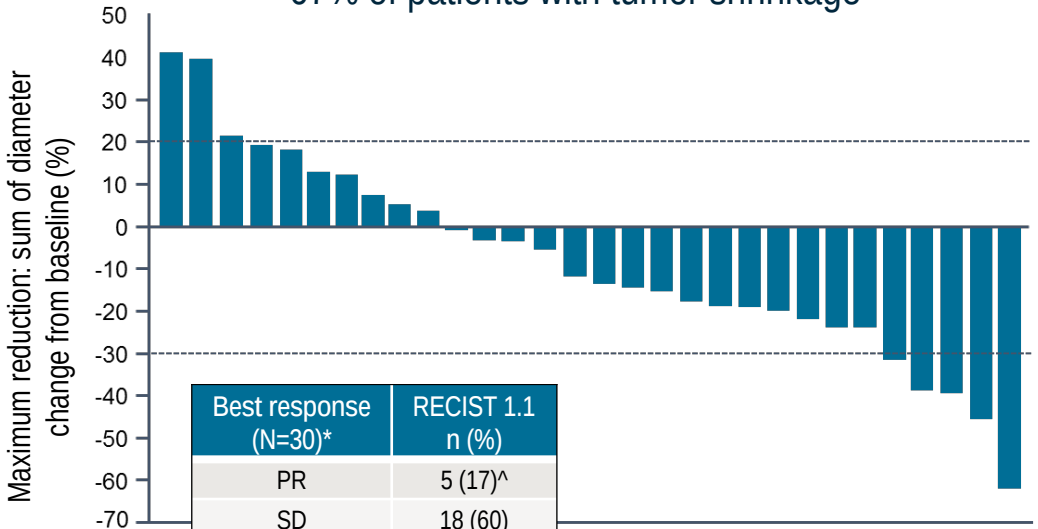
- At least a 20% increase in tumor size
- Or the appearance of 1 or more new tumors

Stable Disease (SD)

- Neither a 30% decrease nor a 20% increase in tumor size

Tumor reduction and prolonged PFS observed in GIST patients with multiple KIT genotypes[1] via central radiology review

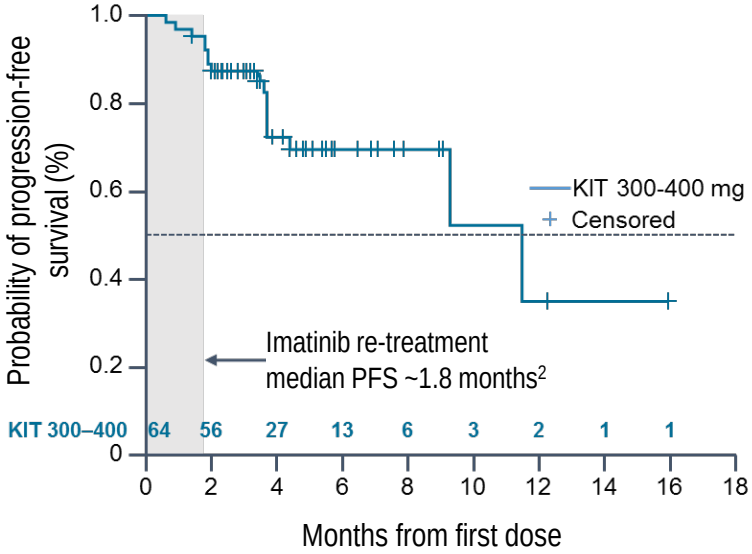
67% of patients with tumor shrinkage



Best response (N=30)*	RECIST 1.1 n (%)
PR	5 (17)^
SD	18 (60)
DCR (PR+SD)	23 (77)
PD	7 (23)

*300 RP2D–400 MTD mg
^2 pending confirmation

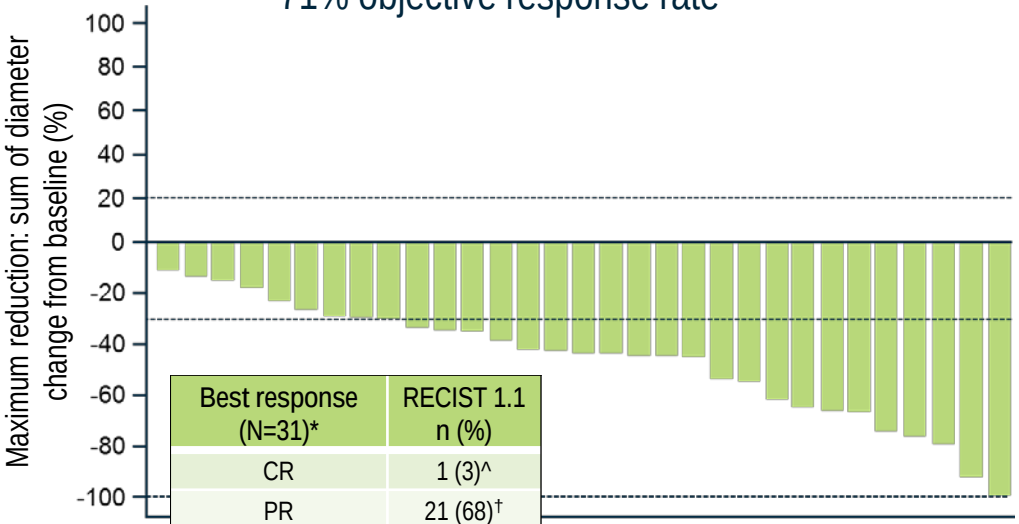
Median PFS 11.5 months; PFS at 6 months 69%



[1] KIT genotypes assessed by archival tumor and ctDNA.[2] Kang et al. Lancet Oncol. 2013;14(12):1175–82.
DCR, disease control rate; MTD, maximum tolerated dose; PD, progressive disease; PR, partial response; RP2D, recommended part 2 dose; SD, stable disease.
Data previously presented in November 2017 at the Connective Tissue Oncology Society (CTOS) Annual Meeting. Data cutoff: October 11, 2017.

Remarkable activity in PDGFRα D842-mutant GIST via central radiology review

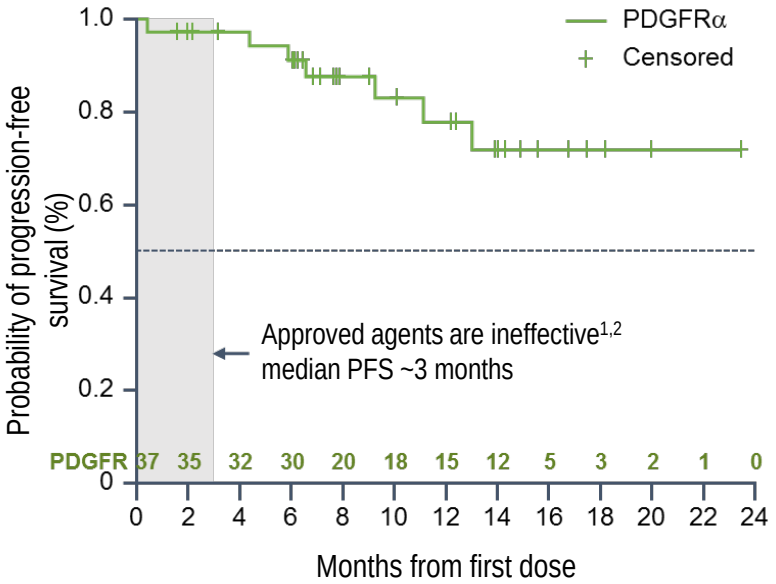
71% objective response rate



Best response (N=31)*	RECIST 1.1 n (%)
CR	1 (3)^
PR	21 (68)†
CR+PR	22 (71)
SD	9 (29)
DCR (CR+PR+SD)	31 (100)
PD	0

*All dose levels included
^PR from C3 to C13, CR at C16, CR pending confirmation
†3 pending confirmation

Median PFS not reached; PFS at 12 months 78%



[1] Cassier et al. Clin Cancer Res. 2012;18(16):4458–64. [2] Yoo et al. Cancer Res Treat. 2016;48(2):546–52
CR, complete response.
Data previously presented in November 2017 at the CTOS Annual Meeting. Data cutoff: October 11, 2017.

Key data conclusions

- Once daily BLU-285 was well tolerated at recommended 300 mg once daily dose
- We observed important anti-tumor activity with BLU-285 in heavily pre-treated KIT-driven GIST at higher dose levels (300 mg or higher)
  - 20 of 30 patients (67%) showed tumor shrinkage
  - Progression free survival of 11.5 months
- BLU-285 showed clinical activity in PDGFRα D842-driven GIST
  - Objective response rate of 71% per central review
  - Median PFS not reached, and progression free survival at 12 months estimated to be 78%

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

Acknowledgments

- First and foremost, we thank the patients and their families for their participation
- In addition – we thank all study investigations, co–investigators, and clinical site staff at the following institutions:
  - Oregon Health & Sciences University
  - Dana-Farber Cancer Institute
  - Royal Marsden Hospital/Institute for Cancer Research
  - University Hospitals Leuven
  - University of Essen
  - Fox Chase Cancer Center
  - Erasmus MC Cancer Institute
  - Centre Leon Berard
  - Institut Gustave Roussy
  - Memorial Sloan Kettering Cancer Center
  - University of Miami Sylvester Comprehensive Cancer Center

Avapritinib clinical development program in GIST is rapidly advancing

Program Status

- ✓ *Favorable tolerability profile*
- ✓ *Strong clinical activity across multiple genotypes*
- ✓ *U.S. FDA Breakthrough Therapy Designation in PDGFRα D842V-driven GIST*
- ✓ *Registration-enabling trials (ongoing or planned)*
- ● *NDA submission in PDGFRα-driven GIST*

Key Next Steps

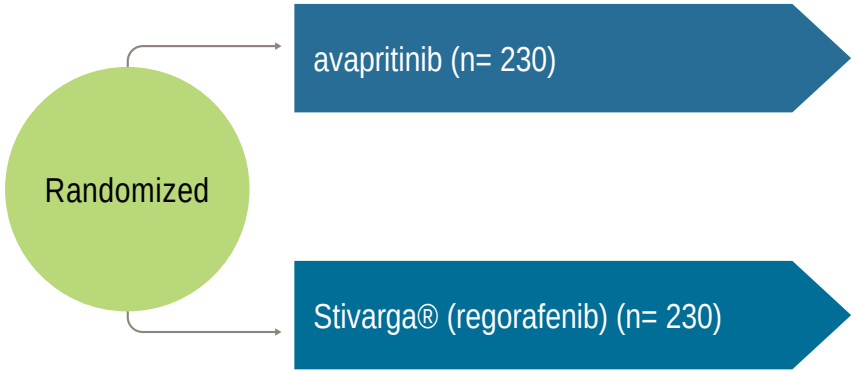
- Completed enrollment of 3L+ (KIT-driven) GIST and PDGFRα-driven GIST cohorts in Phase 1 NAVIGATOR trial in Q1 2018
  - Continue enrollment of 2L GIST cohort in Phase 1 NAVIGATOR trial
- Plan to initiate Phase 3 VOYAGER trial versus regorafenib in 3L GIST in Q2 2018
- Plan to submit initial New Drug Application (NDA) to U.S. FDA for treatment of PDGFRα D842V-driven GIST in 1H 2019
- Explore expedited clinical development pathways for 3L+ GIST with global regulatory authorities

blueprint MEDICINES

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

Planned Phase 3 VOYAGER clinical trial

VOYAGER
GIST



Clinical trial sites in Canada are planned:

Cross Cancer Institute; Edmonton

Jewish General Hospital; Montreal

Princess Margaret Hospital; Toronto

Design

- Open-label, randomized, Phase 3 clinical trial in patients with 3L and 4L GIST
- Patients randomized 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 imatinib and 1 or 2 other tyrosine kinase inhibitors

Primary endpoint

- Progression free survival

blueprint MEDICINES

Questions and Answers

patients@blueprintmedicines.com