

# Safety and Efficacy Results from an Open-label, Multicentre, Phase I/II Study of Avapritinib in Chinese Patients with Gastrointestinal Stromal Tumor (GIST): A Bridging Study of NAVIGATOR

Prof. Jian Li, MD, PhD

Beijing Cancer Hospital, Beijing, China

Jian Li<sup>1</sup>, Xinhua Zhang<sup>2</sup>, Shirong Cai<sup>2</sup>, Yanhong Deng<sup>3</sup>, Xin Wu<sup>4</sup>, Zhichao Zheng<sup>5</sup>, Yongjian Zhou<sup>6</sup>, Yanqiao Zhang<sup>7</sup>, Jun Zhang<sup>8</sup>, Kaixiong Tao<sup>9</sup>, Yuehong Cui<sup>10</sup>, Hui Cao<sup>11</sup>, Kuntang Shen<sup>12</sup>, Jiren Yu<sup>13</sup>, Ye Zhou<sup>14</sup>, Wenxiao Ren<sup>15</sup>, Wanqi Zhao<sup>15</sup>, Jin Hu<sup>15</sup>, Didi Jin<sup>15</sup>, Jianxin Yang<sup>15</sup>, Lin Shen<sup>1</sup>

<sup>1</sup>Beijing Cancer Hospital, Beijing, China; <sup>2</sup>The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; <sup>3</sup>The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; <sup>4</sup>Chinese PLA General Hospital, Beijing, China; <sup>5</sup>Liaoning Cancer Hospital & institute, Shenyang, China; <sup>6</sup>Fujian Medical University Union Hospital, Fuzhou, China; <sup>7</sup>Harbin Medical University Cancer Hospital, Harbin, China; <sup>8</sup>The First Affiliated Hospital of Chongqing Medical University; <sup>9</sup>Wuhan Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; <sup>10</sup>Fudan University Zhongshan Hospital, Shanghai, China; <sup>11</sup>Renji Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China; <sup>12</sup>Fudan University Zhongshan Hospital, Shanghai, China; <sup>13</sup>The First Affiliated Hospital, Zhejiang University, Hangzhou, China; <sup>14</sup>Fudan University Shanghai Cancer Center, Shanghai, China; <sup>15</sup>CStone Pharmaceuticals (Suzhou), Suzhou, China

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# Disclosures

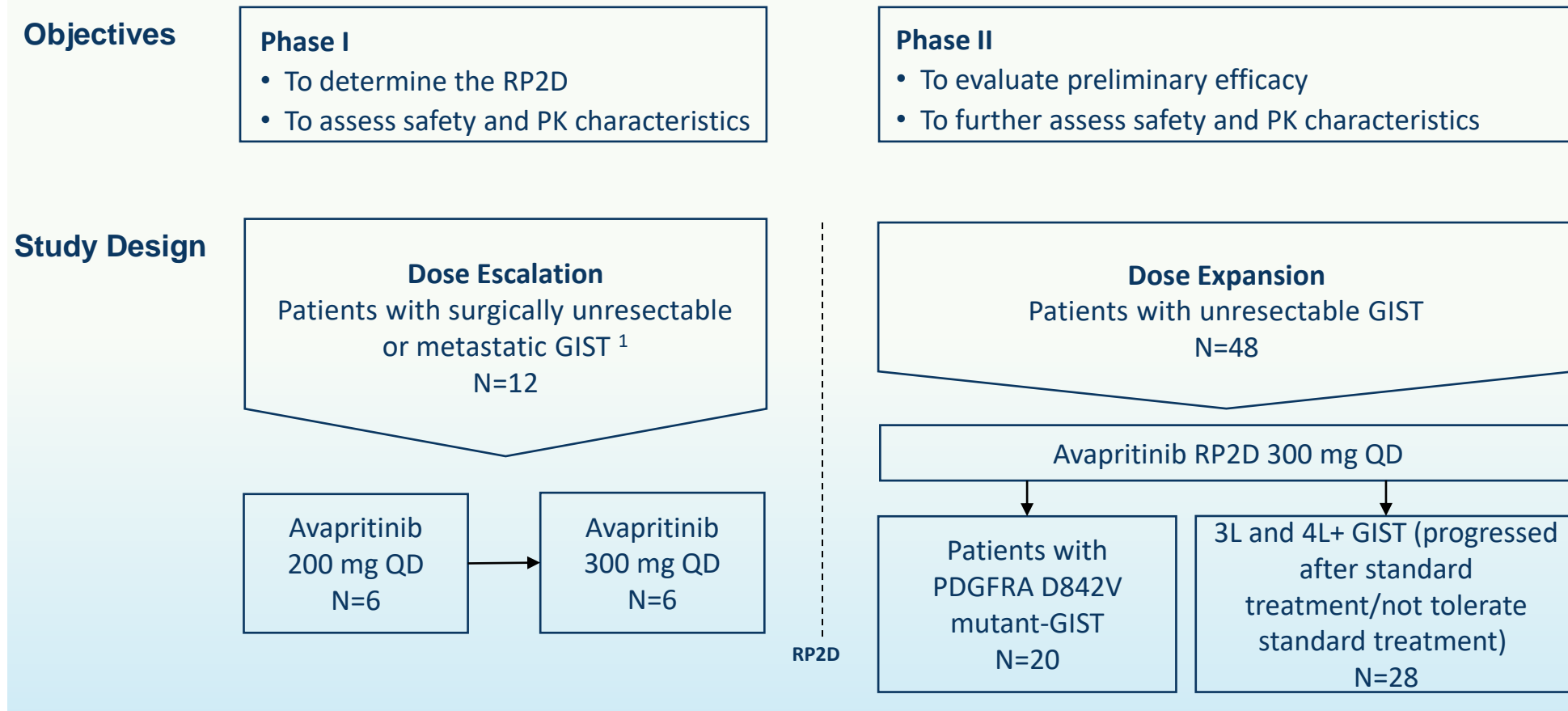
Prof. Jian Li:

- Honoraria as a speaker for CStone Pharmaceuticals, Eli Lilly China, Hengrui Medicine, Innovent Biologics, MSD, Qilu Pharmaceutical, Roche and Sanofi

# Background

- Avapritinib (BLU-285) is a potent, selective, small-molecule inhibitor that targets KIT/PDGFRα activation loop mutants
- Avapritinib is approved in the US based on findings from NAVIGATOR (BLU-285-1101) study
- In March 2021, Avapritinib has been approved in China for the treatment of adult patients with unresectable or metastatic GIST harbouring a PDGFRα exon 18 mutation, including PDGFRα D842V mutations, making it the first approved precision therapy for this population in China
- This presentation reports updated safety and efficacy data from CS3007-101/BLU-285-1105 study, which is a bridging registrational study of NAVIGATOR in China

# Study Design



GIST: gastrointestinal stromal tumor; PK: pharmacokinetics; QD: once daily; RP2D: recommended phase 2 dose

<sup>1</sup> Progression after treatment with imatinib and at least one kind of the other tyrosine kinase inhibitors (TKI), or intolerance of standard treatment, lack of standard treatment, or presence of a D842V mutation in the PDGFRA gene

Data cut-off date: 31 July 2020

# Baseline Characteristics

- As of 31 Jul 2020, a total of 60 patients were treated, 6 received avapritinib 200 mg QD, 54 received avapritinib 300 mg QD
- 40 patients were still on treatment, 10 patients discontinued the treatment due to death, 9 due to disease progression and 1 due to adverse event

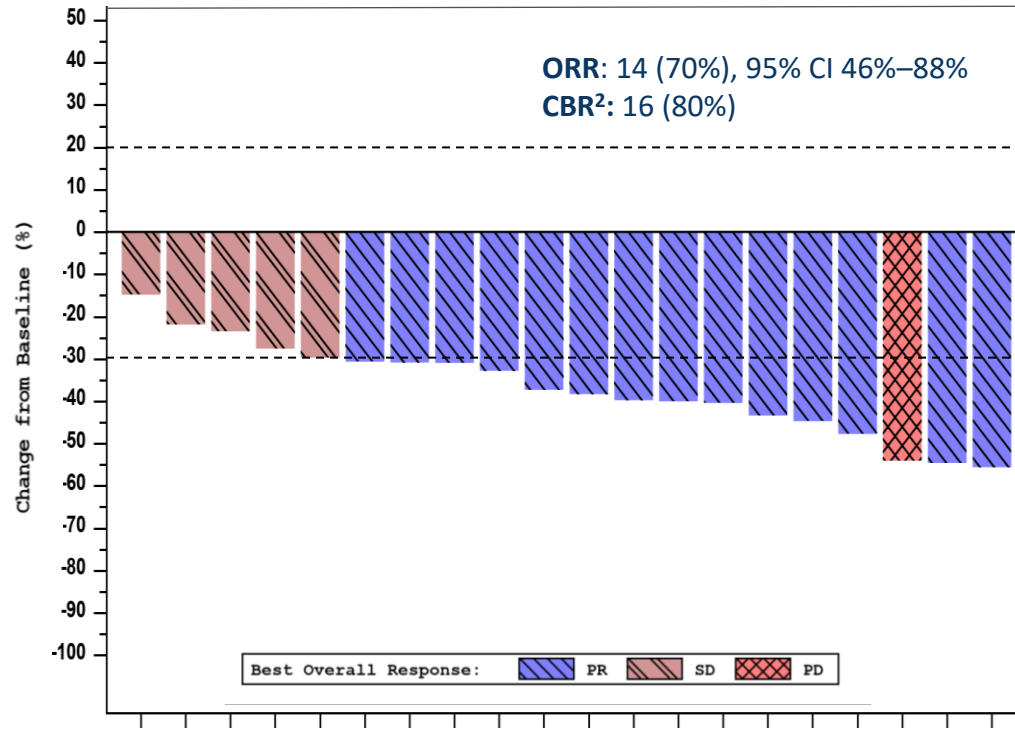
	Avapritinib Starting Dose		
	200 mg N=6	300 mg N=54	Total N=60
Median age (range), years	60 (45-68)	63 (43-70)	63 (43-70)
Male, n (%)	6 (100)	35 (65)	41 (68)
ECOG PS 1	5 (83)	40 (74)	45 (75)
Cancer stage at screening (TNM), Stage IV, n (%)	6 (100)	52 (96)	58 (97)
Metastases diagnosed, Y, n (%)	6 (100)	53 (98)	59 (98)
Time since initial diagnosis (years), Mean (min, max)	6 (2, 10)	6 (0, 16)	6 (0, 16)
Number of previous TKIs, n (%)			
0	0	7 (13)	7 (12)
1	0	10 (19)	10 (17)
2	1 (17)	14 (26)	15 (25)
3	4 (67)	18 (33)	22 (37)
4+	1 (17)	5 (9)	6 (10)
Prior cancer-related Surgery/Procedure, n (%)	6 (100)	53 (98)	59 (98)

ECOG: Eastern Cooperative Oncology Group; PS: performance status; QD: once daily; TKI: tyrosine kinase inhibitor; TNM: tumor, node, metastasis  
Data cut-off date: 31 July 2020

# Efficacy Results

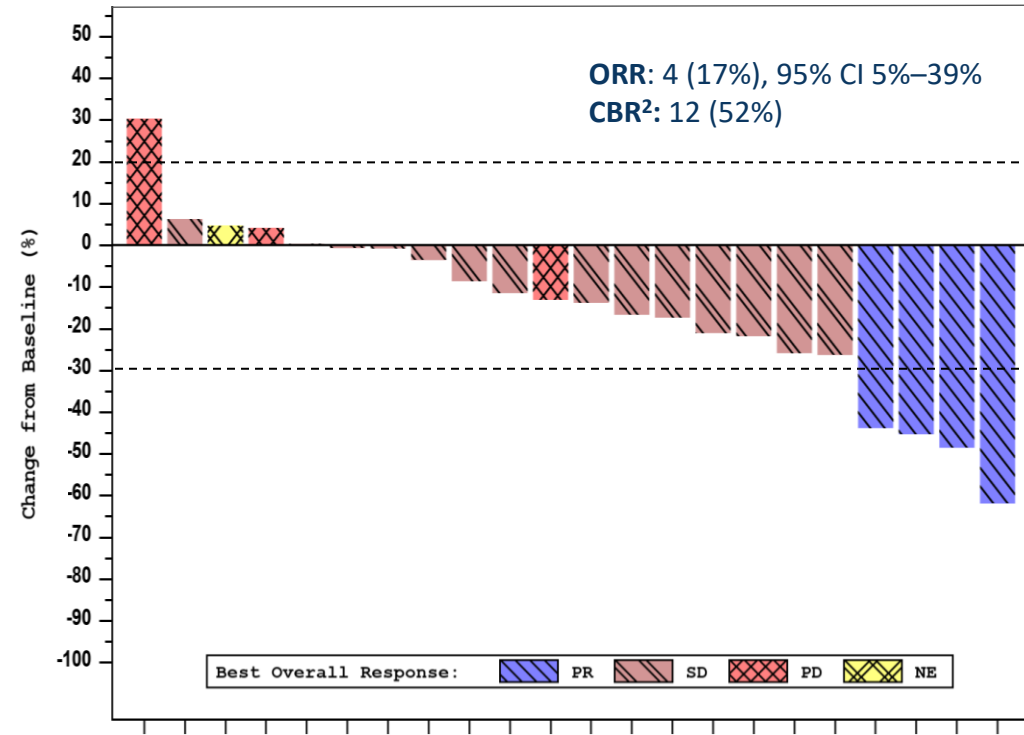
IRRC assessed Best Overall Response<sup>1</sup>

## PDGFRA D842V-mutant GIST Patients with Avapritinib 300 mg QD



Median PFS for PDGFRA D842V-mutant GIST patients was not reached (range:0.03+ to 9.17+)

## 4L+ GIST Patients with Avapritinib 300 mg QD



Median PFS for 4L+ GIST patients was 5.6 months (range: 0.49 to 9.17+)

CBR: clinical benefit rate; CI: confidence incidence; IRRC: independent radiology review committee; ORR: objective response rate; PD: progressive disease; PFS: progression free survival; PR: partial response; QD: once daily; SD: stable disease

One 4L+ GIST patient was classified as not applicable due to no post-baseline response assessment, thus is not shown in the waterfall plot

+ is for the minimum or maximum value from censored patients.

<sup>1</sup> assessed according to mRECIST v1.1

<sup>2</sup> CBR is defined as the proportion of patients with CR/PR or SD lasting  $\geq 4$  cycles from the start of treatment

Data cut-off date: 31 July 2020

# Safety Results

## Most Common TEAEs and AEs of Special Interest

Most common AEs (any cause and grade) in ≥ 20% of patients, n (%)	Avapritinib Starting Dose		
	200 mg N=6	300 mg N=54	200/300 mg N=60
<b>Number of patients with at least one event</b>	<b>6 (100)</b>	<b>54 (100)</b>	<b>60 (100)</b>
Anaemia	5 (83)	47 (87)	52 (87)
Blood bilirubin increased	5 (83)	43 (80)	48 (80)
White blood cell count decreased	5 (83)	29 (54)	34 (57)
Blood creatine phosphokinase increased	6 (100)	23 (43)	29 (48)
Aspartate aminotransferase increased	4 (67)	23 (43)	27 (45)
Face oedema	1 (17)	25 (46)	26 (43)
Eyelid oedema	6 (100)	19 (35)	25 (42)
Neutrophil count decreased	2 (33)	19 (35)	21 (35)
Hair colour changes	1 (17)	18 (33)	19 (32)
Hypokalaemia	2 (33)	15 (28)	17 (28)
Oedema peripheral	5 (83)	12 (22)	17 (28)
Periorbital oedema	0	16 (30)	16 (27)
Hypocalcaemia	3 (50)	12 (22)	15 (25)
Nausea	0	13 (24)	13 (22)
Alanine aminotransferase increased	2 (33)	10 (19)	12 (20)
Hypophosphataemia	1 (17)	11 (20)	12 (20)

AESI (any cause and grade), n (%)	Avapritinib Starting Dose		
	200 mg N=6	300 mg N=54	200/300 mg N=60
<b>Number of patients with at least one event</b>	<b>0</b>	<b>6 (11)</b>	<b>6 (10)</b>
Cognitive effects	0	6 (11)	6 (10)
Memory impairment	0	4 (7)	4 (7)
Cognitive disorder	0	2 (4)	2 (3)
Confusional state	0	0	0
Encephalopathy	0	0	0
Intracranial bleeding	0	0	0

- The median treatment duration was 25 (range: 2-49) weeks for the total safety population
- 59 (98%) patient reported treatment-related AEs, with the most common reported being anaemia (45, 75%)
- 41 (68%) patients had Grade ≥3 treatment-related AEs
- 41 (68%) patients reported AEs leading to drug interruption
- 11 (18%) patient reported AEs leading to death (mostly were disease progression, 7, 12%)
- A total of 6 (10%) patients experienced AESI, they all reported cognitive effects

# Conclusions

- Avapritinib as a precise target therapy provided promising clinical benefit in Chinese patients with PDGFRA D842V-mutant GIST, a GIST subtype that has a low response rate and poor clinical outcome when treated with other available kinase inhibitors
  - IRRC-assessed ORR was 70%, CBR was 80%, median PFS was not reached
- Avapritinib has moderate clinical activity in fourth- and later-line (4L+) treatment of Chinese patients with GIST, making it a potential new treatment option for these population
  - IRRC-assessed ORR was 17%; CBR was 52%; median PFS was 5.6 months
- Avapritinib demonstrated a tolerable safety profile in Chinese patients with GIST, consistent with the results seen in the global study



# Acknowledgement

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