Efficacy and Safety of Pralsetinib in Chinese Patients with Advanced RET Fusion+ Non-Small Cell Lung Cancer

Qing Zhou[1], Yi-Long Wu[1], Jianhua Chang[2], Huijie Wang[2], Yun Fan[3], Jun Zhao[4], Gang Wu[5], Yuping Sun[6], Meili Sun[6], Xiangcai Wang[7], Huaqiu Shi[7], Weiqi Nian[8], Ke Wang[9], Xiangqian Zheng[10], Lili Qu[11], Sheng Yao[11], Zhenwei Shen[11], Peiqi Li[11], Jason Yang[11]

1. Guangdong Lung Cancer Institute, Guangdong Provincial Key Laboratory of Translational Medicine in Lung Cancer, Guangdong Provincial People's Hospital & Guangdong Academy of Medical Sciences, Guangzhou, China. 2.Fudan University Shanghai Cancer Center, Shanghai, China. 3.Zhejiang Cancer Hospital, Hangzhou, China. 4. Beijing Cancer Hospital, Beijing, China. 5.Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China. 6.Jinan Central Hospital, Shandong University, Jinan, China. 7. First Affiliated Hospital of Gannan Medical University, Ganzhou, China. 8.Chongqing Cancer Hospital, Chongqing, China. 9.West China Hospital Sichuan University, Chengdu, China. 10.Tianjin Medical University Cancer Institute & Hospital, Tianjin, China. 11. CStone Pharmaceuticals (Su Zhou) Co., Ltd., Suzhou, China.

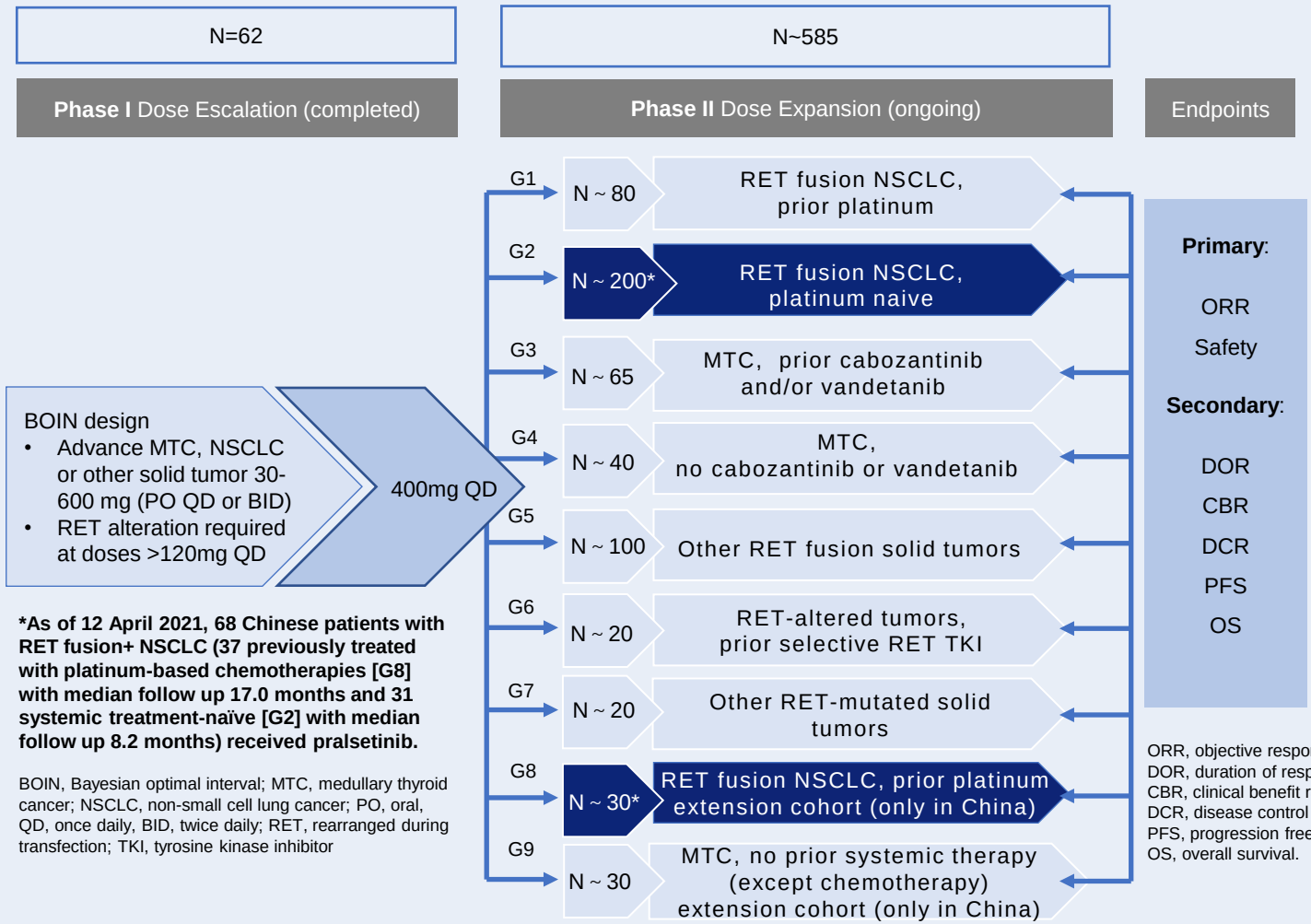
Disclosure Information of Prof. Qing Zhou

Ineligible Company	Relationship(s)
AstraZeneca, Roche	Honorarium received from promotional activities

1 Background

- RET fusions have been reported as oncogenic drivers in approximately 1% to 2% of non-small cell lung cancer (NSCLC) patients[1-4].
- Pralsetinib is a highly potent and selective rearranged-during-transfection (RET) kinase inhibitor targeting oncogenic RET alterations, including RET fusions[5-6].
- U.S. FDA granted accelerated approval to pralsetinib in 2020 for the treatment of adults with metastatic RET fusion+ NSCLC and patients with advanced RET fusion+ thyroid cancer and RET-mutant medullary thyroid cancer.
- China NMPA approved pralsetinib in 2021 for the treatment of adults with locally advanced or metastatic RET fusion+ NSCLC who previously received platinum-based chemotherapy.
- A global phase I/II study “ARROW” (BLU-667-1101; NCT03037385) has showed broad and durable antitumor activity of pralsetinib in a variety of advanced RET-altered solid tumors, including RET fusion+ NSCLC.
- The primary analysis reported at WCLC 2020 has shown that pralsetinib provides rapid, durable tumor responses, and shows a well-tolerated safety profile in a cohort of Chinese patients with RET fusion+ NSCLC who received prior platinum-based chemotherapy.
- Here we present the efficacy and safety results of pralsetinib in both treated and treatment-naive Chinese patients with RET fusion+ NSCLC.

2 ARROW Study Design



***As of 12 April 2021, 68 Chinese patients with RET fusion+ NSCLC (37 previously treated with platinum-based chemotherapies [G8] with median follow up 17.0 months and 31 systemic treatment-naïve [G2] with median follow up 8.2 months) received pralsetinib.**

BOIN, Bayesian optimal interval; MTC, medullary thyroid cancer; NSCLC, non-small cell lung cancer; PO, oral, QD, once daily, BID, twice daily; RET, rearranged during transfection; TKI, tyrosine kinase inhibitor

ORR, objective response rate; DOR, duration of response; CBR, clinical benefit rate; DCR, disease control rate; PFS, progression free survival; OS, overall survival.

1.Mulligan LM. Nat Rev Cancer. 2014;14:173–186; 2. Kohno T et al. Nat Med. 2012;18:375–377; 3. Lipson D et al. Nat Med. 2012;18:382–384; 4. Takeuchi K et al. Nat Med. 2012;18:378–381; 5. Subbiah V et al. Cancer Discov. 2018;8:836–849; 6. Evans E et al. J Thoracic Oncol. 2019;14:S701

Data cut-off: April 12, 2021

Demographics and Baseline Characteristics

Characteristic	NSCLC patients in Chinese cohort	
	Prior platinum treatment (n=37)	No prior systemic treatment (n=31)
Age, years, median (range)	54 (26,77)	57 (30,79)
Sex, male, n (%)	17 (46)	11 (35.5)
Race, Asian, n (%)	37 (100)	31 (100)
ECOG performance status, n (%)		
0	2 (5.4)	1 (3.2)
1	35 (94.6)	30 (96.8)
Histology type, n (%)		
Adenocarcinoma	36 (97.3)	31 (100)
Other	1 (2.7)	0
CNS metastasis, n (%)	15 (40.5)	8 (25.8)
Tumour stage at screening, n (%)		
Stage IIIB	0	1 (3.2)
Stage IIIC	0	1 (3.2)
Stage IVA	8 (21.6)	12 (38.7)
Stage IVB	29 (78.4)	17 (54.8)
Number of prior regimens, n (%)		
1	14 (37.8)	0
2	5 (13.5)	0
≥3	18 (48.6)	0
Smoking history, n (%)		
Never smoked	25 (67.6)	21 (67.7)
Former	11 (29.7)	10 (32.3)
Current	1 (2.7)	0
RET – Fusion Partner, n (%)		
KIF5B	23 (62.2)	22 (71.0)
CCDC6	7 (18.9)	5 (16.1)
Other	7 (18.9)	4 (12.9)

ECOG, Eastern Cooperative Oncology Group;
CNS, Central Nervous System;
RET, rearranged during transfection;

Data cut-off: April 12, 2021

Efficacy Summary

Pralsetinib demonstrated robust anti-tumor activities in RET fusion+ NSCLC patients regardless of prior therapies

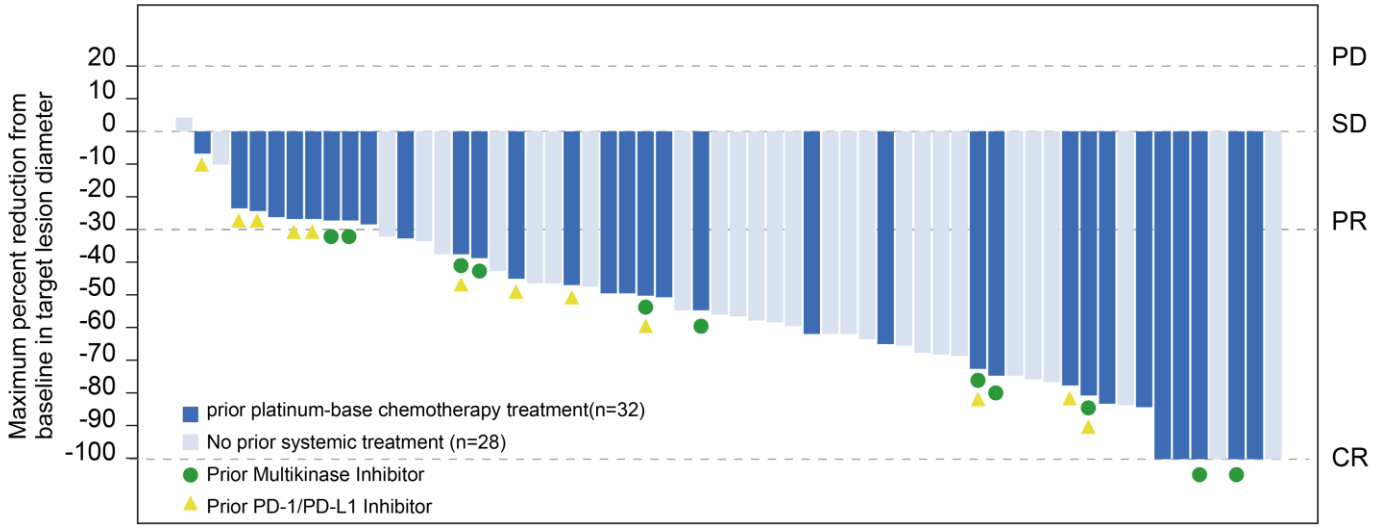
Response Summary of Patients with Measurable Baseline Disease per BICR

Outcome	NSCLC patients in Chinese cohort	
	Prior platinum-based chemotherapy treatment (n=33)	No prior systemic treatment (n=30)
Confirmed ORR, n(%) [95% CI]	22 (66.7) [48.2-82.0]	24 (80.0) [61.4-92.3]
CR, n(%)	1 (3.0)	2 (6.7)
PR, n(%)	21 (63.6)	22 (73.3)
SD, n(%)	9 (27.3)	2 (6.7)
PD, n(%)	1 (3.0)	2 (6.7)
NE, n(%)	1 (3.0)	2 (6.7)
***CBR, % (95% CI)**	84.8 (68.1-94.9)	86.7 (69.3-96.2)
DCR, % (95% CI)	93.9 (79.8-99.3)	86.7 (69.3-96.2)

*Confirmed CR, PR or SD >=16 Weeks

BICR, Blinded Independent Centralized Review; ORR, objective response rate; CI, confidence interval; CR, complete response; PR, partial response; SD, stable disease; PD, progress of disease; NE, not evaluable; CBR, clinical benefit rate; DCR, disease control rate;

Maximum Tumor Shrinkage in Target Lesion (N=60)**



** 3 patients were not included due to absence of evaluable post-baseline disease response assessment by BICR per RECIST v1.1

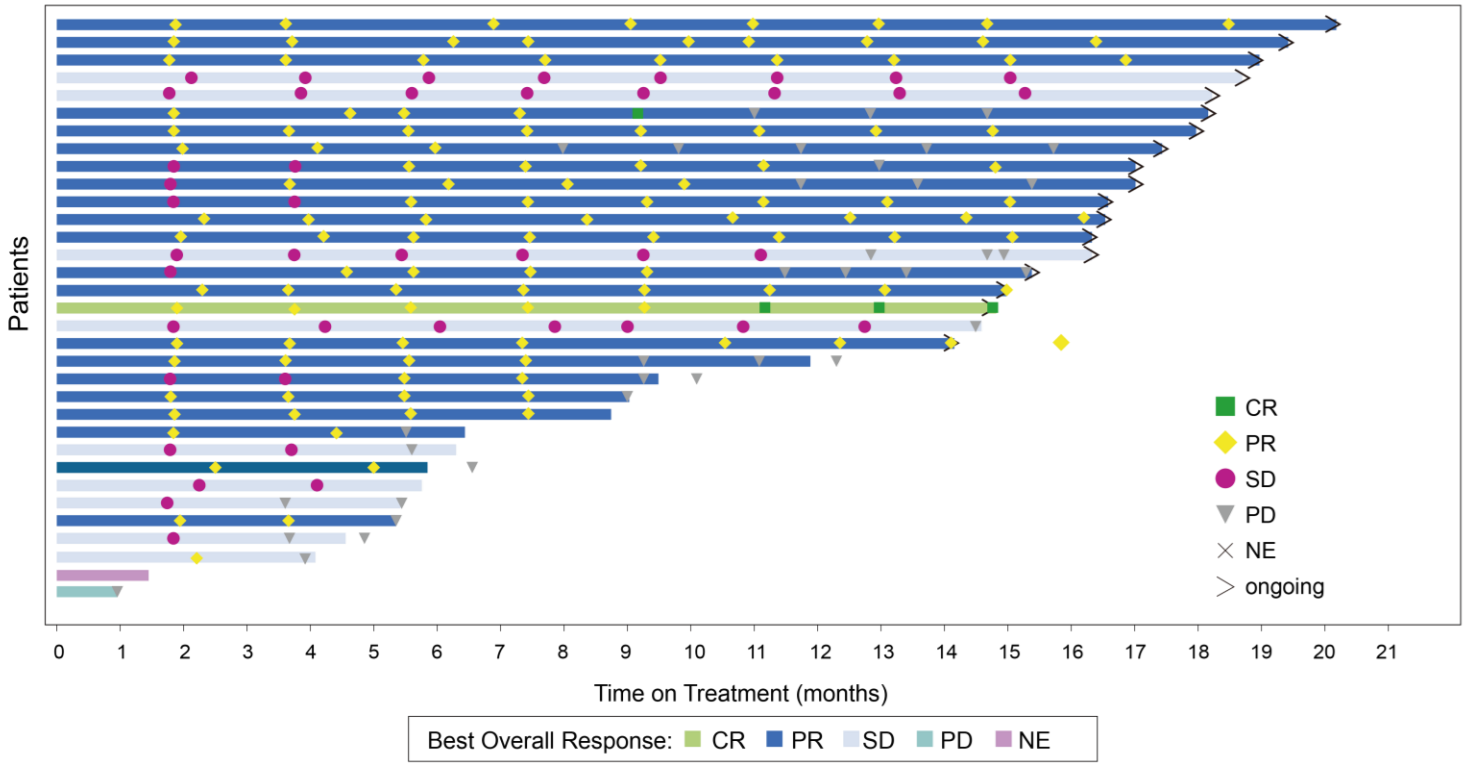
PD, progress of disease; SD, stable disease; PR, partial response; CR, complete response.

Data cut-off: April 12, 2021

Efficacy Summary

Pralsetinib induces rapid and durable response in RET fusion+ advanced NSCLC in Chinese cohort

Group 8 (NSCLC after prior platinum-based chemotherapy): Duration of Treatment and Response (N=33)



CR, complete response; PR, partial response; SD, stable disease; NE, not evaluable;

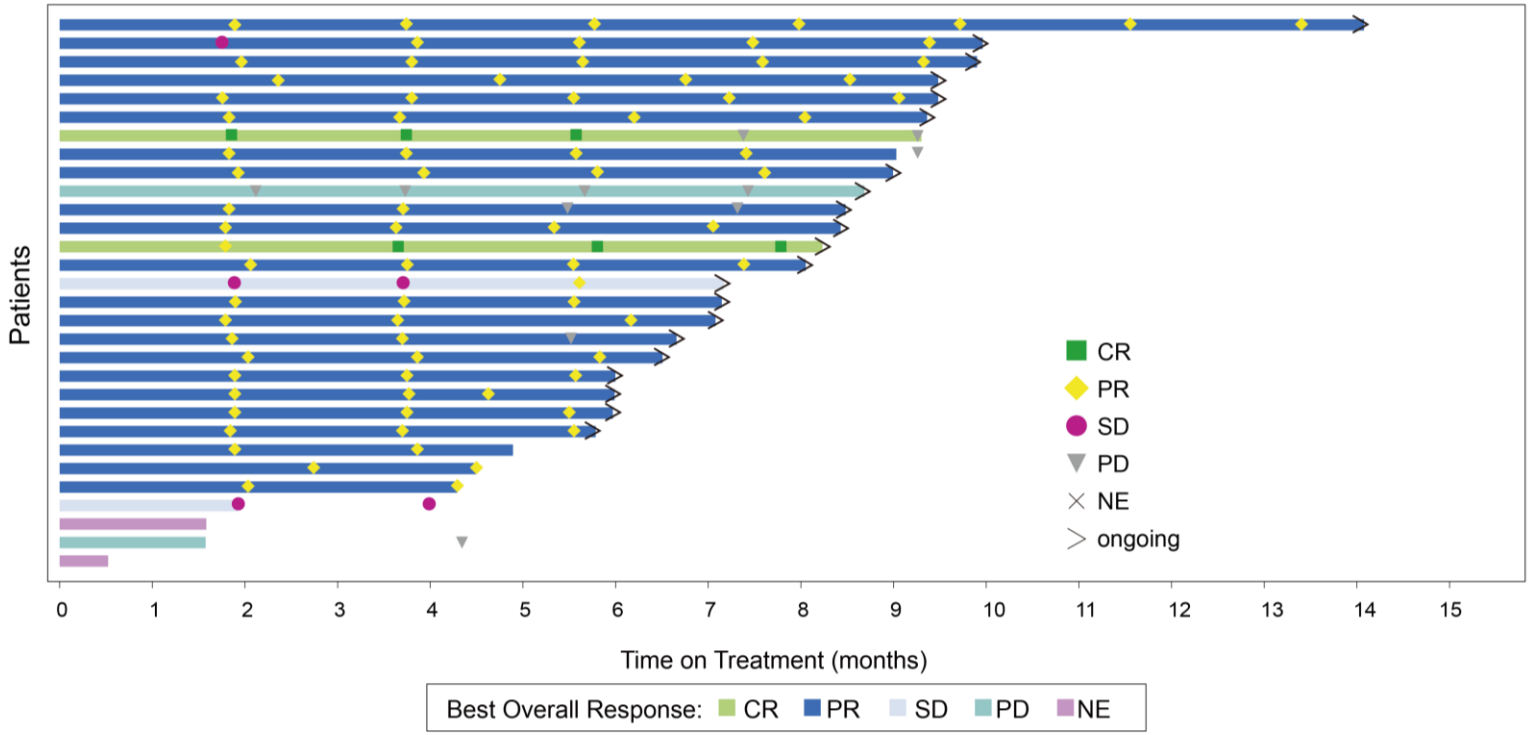
- Median follow up was 17.0 (range: 16.3-18.1) months.
- Median treatment duration was 14.65 (range: 0.9-20.0) months.
- 68.18% (15/22) of responders remain on treatment.
- Median time to first response among the 22 responders was 1.89 (1.7-5.6) months.
- 6-month and 9-month DOR rates were 77.3% (95% CI: 59.8-94.8) and 50.0% (95% CI: 29.1-70.9), respectively.

Data cut-off: April 12, 2021

Efficacy Summary

Pralsetinib induces rapid and durable response in RET fusion+ advanced NSCLC in Chinese cohort

Group 2 (treatment-naive NSCLC): Duration of Treatment and Response (N=30)



CR, complete response; PR, partial response; SD, stable disease; NE, not evaluable;

- Median follow up was 8.2 (range: 7.1-8.6) months.
- Median treatment duration was 7.13 (range: 0.5-14.0) months.
- 79.17% (19/24) of responders remain on treatment.
- Median time to first response among the 24 responders was 1.87 (1.7-3.8) months.
- 6-month and 9-month DOR rates were 76.7% (95% CI: 55.6-97.8) and 38.3% (95% CI: 0.0-92.5), respectively.

Data cut-off: April 12, 2021

Safety Overview

Pralsetinib well tolerated in Chinese patients with RET fusion+ NSCLC with a manageable safety profile

Treatment-Related AEs in ≥ 20% of Patients

Preferred Term	Overall (N=68)	
	Any grade, n (%)	Grade 3-4, n (%)
Aspartate aminotransferase increased	55 (80.9)	3 (4.4)
Neutrophil count decreased	54 (79.4)	23 (33.8)
Anaemia	46 (67.6)	22 (32.4)
White blood cell count decreased	41 (60.3)	9 (13.2)
Alanine aminotransferase increased	39 (57.4)	3 (4.4)
Blood creatine phosphokinase increased	31 (45.6)	12 (17.6)
Hypertension	24 (35.3)	8 (11.8)
Platelet count decreased	21 (30.9)	6 (8.8)
Blood creatinine increased	20 (29.4)	1 (1.5)
Bilirubin conjugated increased	19 (27.9)	0
Constipation	19 (27.9)	0
Gamma-glutamyltransferase increased	19 (27.9)	4 (5.9)
Blood alkaline phosphatase increased	18 (26.5)	2 (2.9)
Malaise	17 (25.0)	0
Blood bilirubin increased	16 (23.5)	1 (1.5)
Hypocalcaemia	14 (20.6)	1 (1.5)

- All 68 patients experienced at least one treatment emergent adverse event
- 67/68 (98.5%) patients experienced treatment-related adverse events (TRAEs).
- 7/68 (10.3%) patients discontinued from treatment due to TRAE.

Additional Grade 3-4 TRAEs(≥5%):
- Lymphocyte count decreased (5.9%)
- Leukopenia (5.9%)
- Hypophosphataemia (11.8%)

Data cut-off: April 12, 2021

Conclusions

- Pralsetinib is a promising targeted therapy with rapid and durable clinical activity in Chinese patients with RET fusion+ NSCLC regardless of prior therapies.
- Efficacy results observed in Chinese population are consistent with those previously reported from the global population in the ARROW trial.
- Pralsetinib safety profile in Chinese patients is manageable, with no new safety signals detected.
- Pralsetinib, with a favorable benefit-risk profile, represents an efficacious treatment option and demonstrates the potential of being a new Standard-of-Care to Chinese patients with RET-fusion driven advanced NSCLC.

Data cut-off: April 12, 2021

ACKNOWLEDGEMENTS

- Patients and their families
- Investigators and site research staffs
- This study is sponsored by CStone Pharmaceuticals (Suzhou) Co. Ltd. and Blueprint Medicines Corporation