



# Efficacy and Safety of Pralsetinib, a Selective RET Inhibitor, in Chinese Patients with Advanced RET-mutant Medullary Thyroid Cancer

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# Disclosures

**Prof. Ming Gao**  
**has no interest to declare.**

# Learning Objectives



**Pralsetinib may provide a potent targeted treatment option for Chinese MTC patients with RET mutation.**



**Pralsetinib showed broad and durable anti-tumor activity in Chinese patients with advanced or metastatic RET-mutant MTC, consistent with previously reported results in the global ARROW study.**



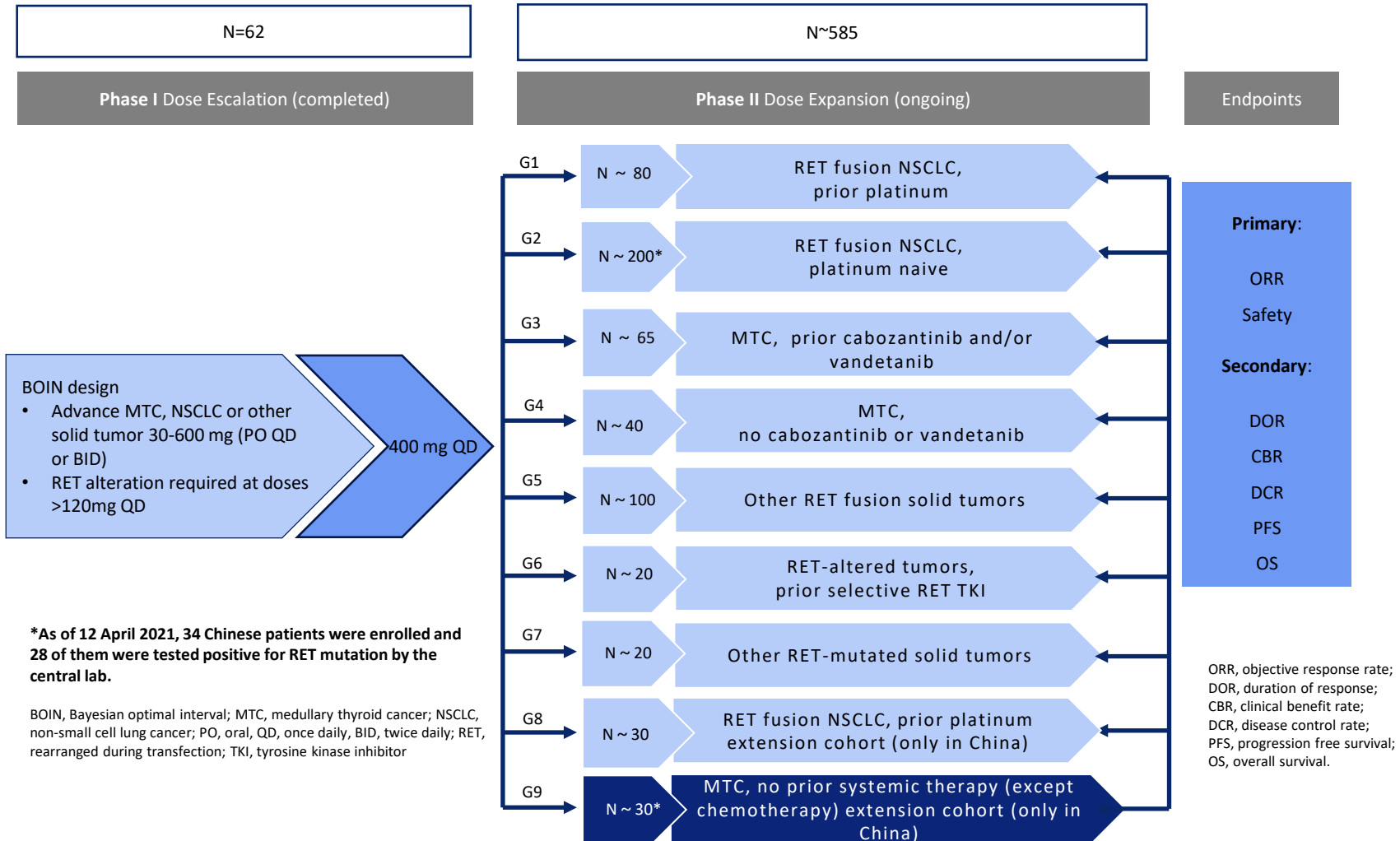
**Safety profile of pralsetinib in Chinese patients was manageable, no new safety signals detected.**

# Background

- Medullary thyroid cancer (MTC) accounts for 1-5% of thyroid cancers. RET mutations are present in 50–90% of sporadic MTC and nearly 100% of germline MTC cases as part of MEN2 syndrome<sup>1</sup>.
- Pralsetinib is a potent and selective rearranged during transfection (RET) kinase inhibitor designed to target oncogenic RET, including RET mutations<sup>2-3</sup>.
- U.S. FDA granted accelerated approval to pralsetinib in 2020 for the treatment of adults and pediatric patients 12 years of age and older with metastatic RET-fusion NSCLC and patients with advanced RET-fusion thyroid cancer and RET-mutant MTC.
- 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-mutant MTC<sup>4-5</sup>.
- Here we present the efficacy and safety results of pralsetinib in Chinese patients with RET-mutant MTC.

1. Subbiah V et al. Cancer Discov. 2020;38:1209–1221; 2. Subbiah V et al. Cancer Discov. 2018;8:836–849; 3. Evans E et al. J Thoracic Oncol. 2019;14:S701; 4. Hu M et al. presented at European Society for Medical Oncology, October, 2020; 5. Subbiah V et al. presented at American Society of Clinical Oncology, May, 2020.

# ARROW Study Design



Data cut-off: April 12, 2021

# Demographics and Baseline Characteristics

Characteristic	RET-mutation MTC patients in Group 9 (N=28)
Age, years, median (range)	51.0 (19, 66)
Sex, male, n (%)	16 (57.1)
Race, Asian, n (%)	28 (100)
ECOG performance status, n (%)	
0	12 (42.9)
1	16 (57.1)
CNS metastasis, n (%)	0
Tumour stage at screening, n (%)	
Stage IV	1 (3.6)
Stage IVC	27 (96.4)
Prior antineoplastic therapy, n (%)	
Yes	1 (3.6) <sup>[1]</sup>
No	27 (96.4)
RET - mutation, n (%)	
M918T	18 (64.3)
Cysteine rich domain <sup>[2]</sup>	6 (21.4)
V804X <sup>[3]</sup>	0
Other	4 (14.3)

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

[1] Chemotherapy.

[2] Cysteine rich domain includes patients with single nucleotide variants of or short indels that include but are not limited to the following residues: C609, C611, C618, C620, C630 and/or C634 of RET.

[3] V804X includes patients with a RET-mutation status of V804M and/or V804L

# Efficacy Summary

## Pralsetinib showed broad anti-tumor activity in Chinese patients with RET - mutant MTC

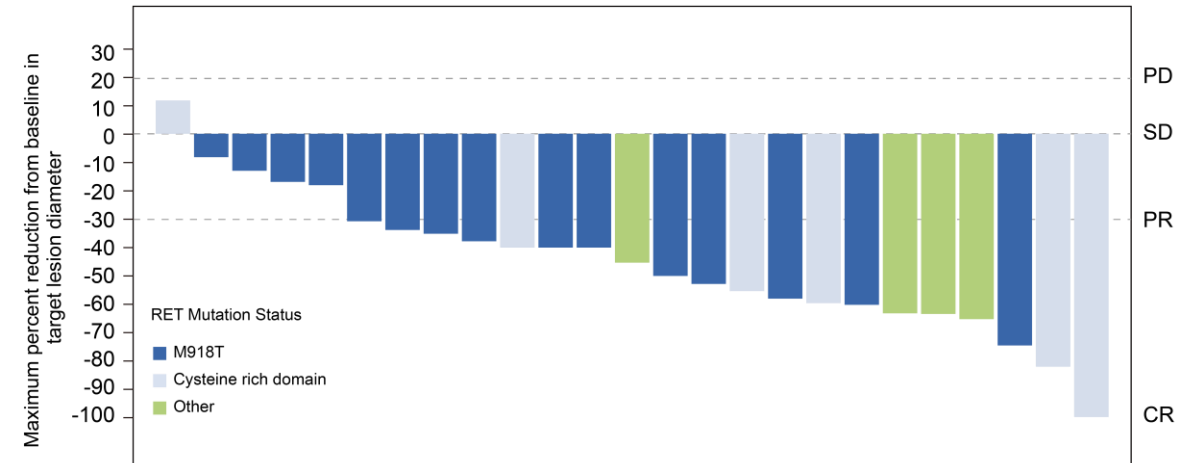
### Response Summary of Patients with Measurable Baseline Disease per BICR

Outcome	RET-mutant MTC patients in Group 9 (N=26)
Confirmed ORR, n(%) (95% CI)	19 (73.1) (52.2-88.4)
CR, n(%)	3 (11.5)
PR, n(%)	16 (61.5)
SD, n(%)	3 (11.5)
PD, n(%)	3 (11.5)
NE, n(%)	1 (3.8)
CBR*, % (95% CI)	76.9 (56.4-91.0)
DCR, % (95% CI)	84.6 (65.1-95.6)

\*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 Lesions (N=25\*\*)



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

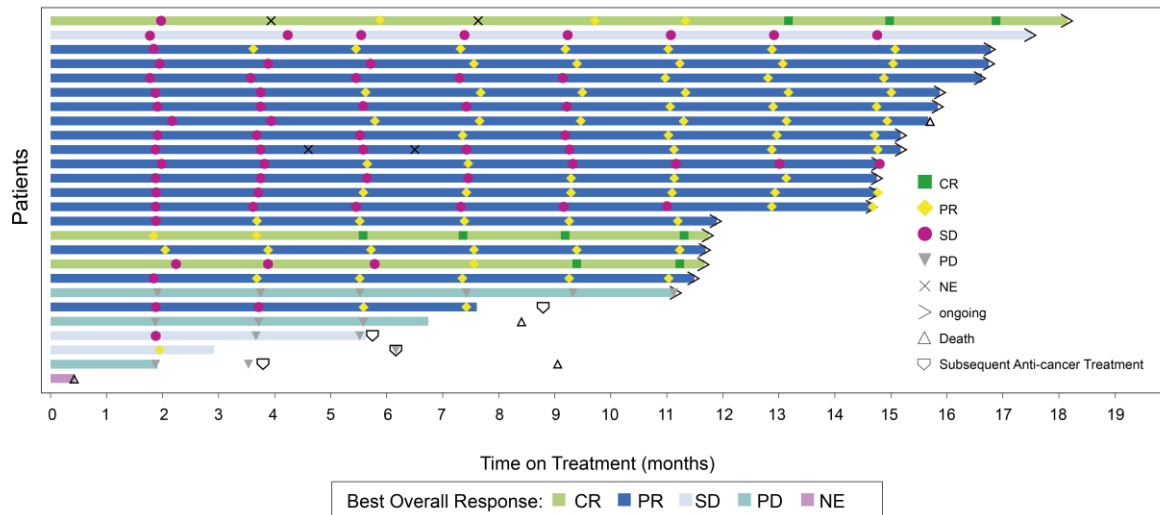
PD, progress of disease; SD, stable disease; PR, partial response; CR, complete response.

Data cut-off: April 12, 2021

# Efficacy Summary

## Pralsetinib induced durable response in Chinese patients with RET - mutant MTC

### Group 9 (RET - mutant MTC patients): Duration of Treatment and Responses (N=26)



- Median follow up was 14.8 (95% CI: 12.4, 15.8) months.
- Median treatment duration was 14.7 (range: 0.4-18.1) months.
- Median time to response was 5.8 (range: 1.8-12.8) months.

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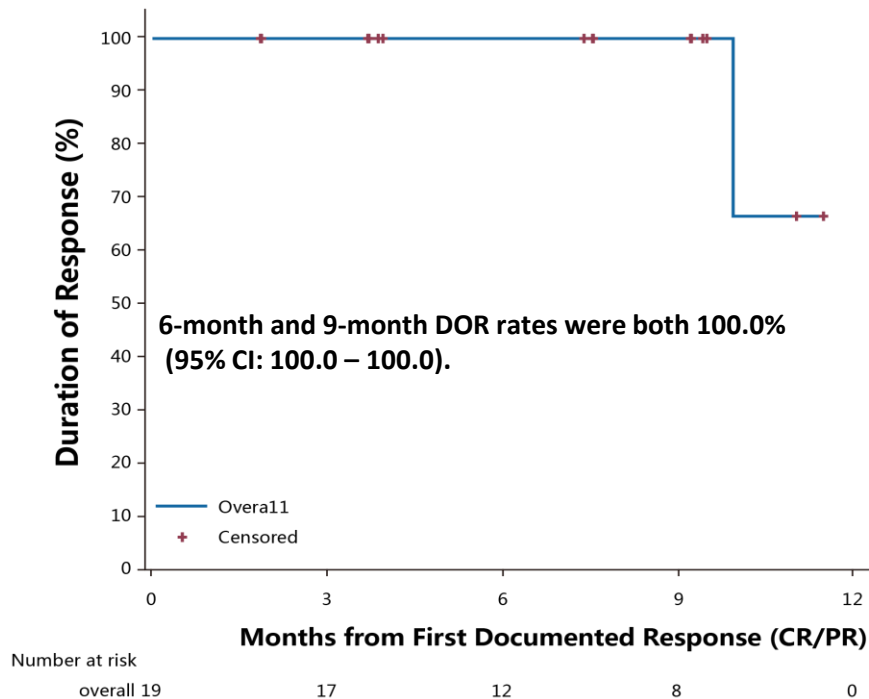
CR, complete response; PR, partial response; SD, stable disease; NE, not evaluable.



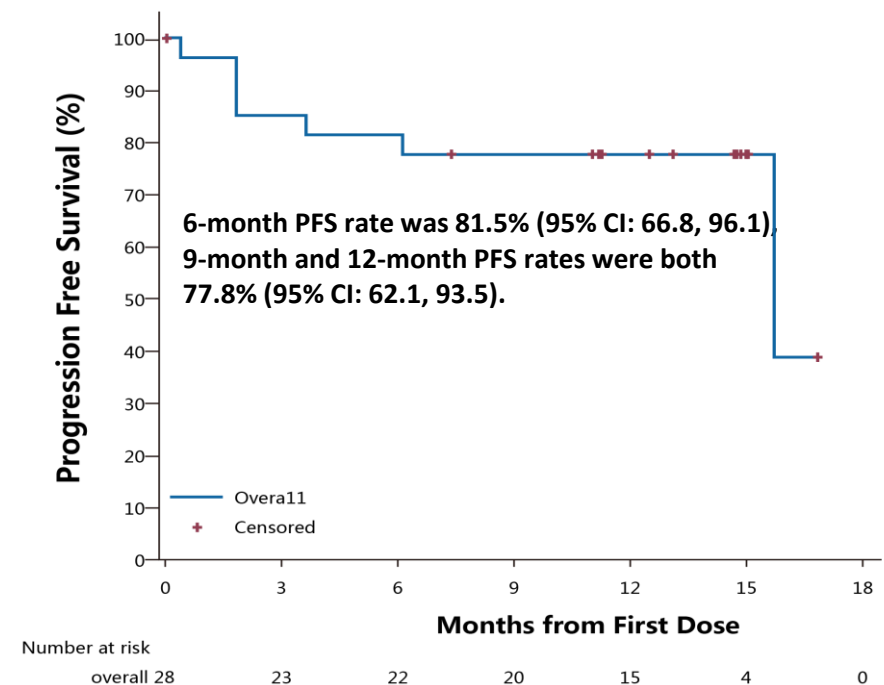
# BICR-Assessed DOR and PFS (RECIST v1.1)

Pralsetinib provided prolonged DOR and PFS in Chinese patients with RET - mutant MTC

## DOR



## PFS



DOR presented for efficacy population and included confirmed responses only; PFS presented for efficacy population.  
BICR, Blinded Independent Central Review; DOR, duration of response; PFS, progression free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

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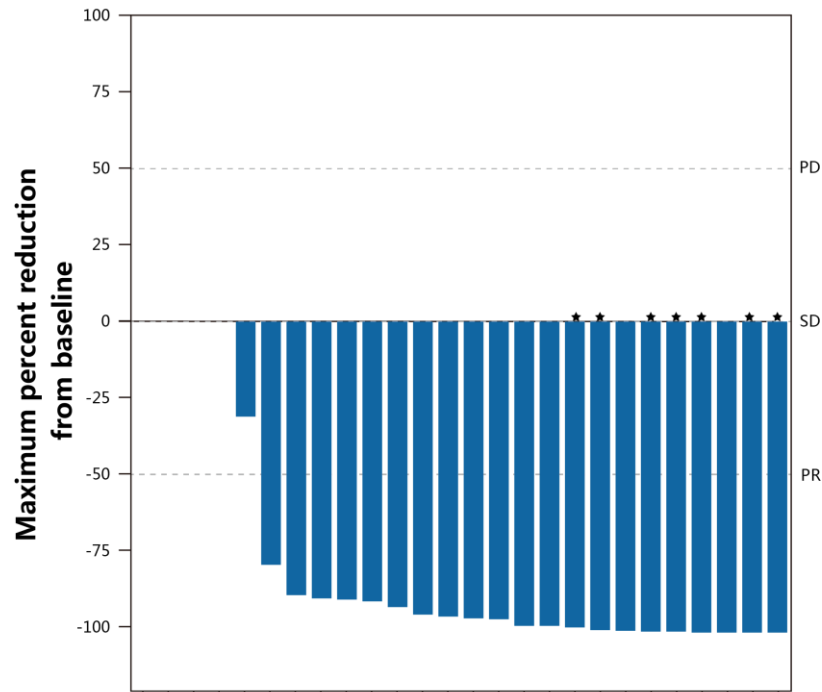


# Biochemical response

Pralsetinib induced substantial biochemical response in Chinese patients with RET - mutant MTC

## Calcitonin

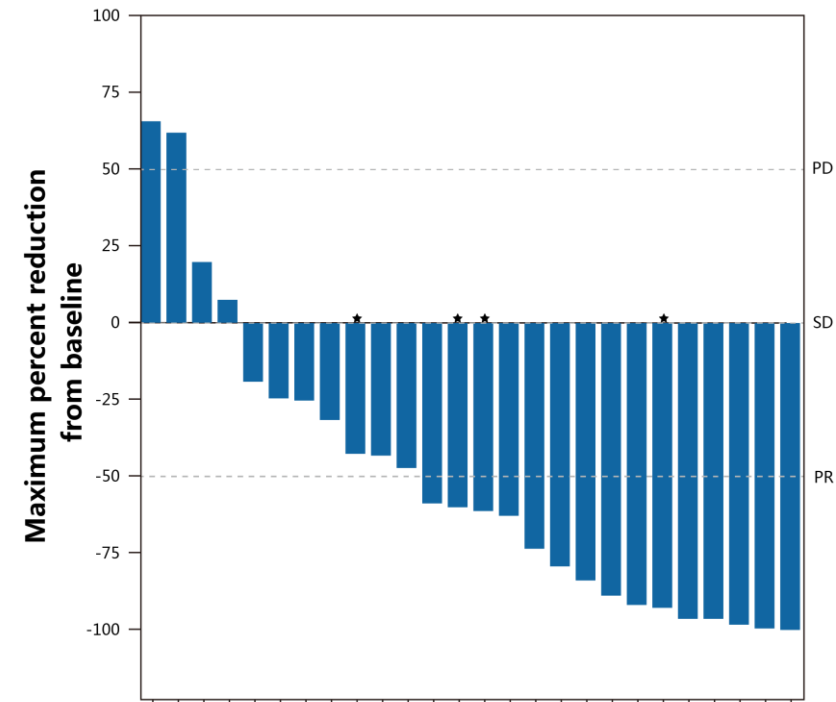
Biochemical response rate of calcitonin was 71.4% (95 CI: 51.3, 86.8)



MTC, medullary thyroid cancer; CEA, carcinoembryonic antigen.  
\*patient with complete response.

## Carcinoembryonic Antigen (CEA)

Biochemical response rate of CEA was 53.8% (95 CI: 33.4, 73.4)



# Safety Overview

**Pralsetinib was generally well tolerated in Chinese patients with RET- mutant MTC**

Preferred Term	Overall (N=28)	
	Any grade (≥ 20%), n (%)	Grade 3-4, n (%)
Hyperphosphataemia	16 ( 57.1)	0
White blood cell count decreased	16 ( 57.1)	4 (14.3)
Aspartate aminotransferase increased	15 ( 53.6)	0
Neutrophil count decreased	15 ( 53.6)	8 (28.6)
Blood lactate dehydrogenase increased	14 ( 50.0)	0
Blood creatine phosphokinase increased	13 ( 46.4)	6 (21.4)
Alanine aminotransferase increased	12 ( 42.9)	1 (3.6)
Constipation	11 ( 39.3)	0
Hypocalcaemia	11 ( 39.3)	3 (10.7)
Anaemia	10 ( 35.7)	3 (10.7)
Hypoalbuminaemia	8 ( 28.6)	0
Weight increased	8 ( 28.6)	0
Blood creatinine increased	7 ( 25.0)	0
Hypertension	7 ( 25.0)	3 (10.7)
Lymphocyte count decreased	7 ( 25.0)	5 (17.9)

- All patients experienced at least one treatment emergency adverse event (TEAE) and treatment related adverse event (TRAE).
- 22 (78.6%) patients experienced Grade 3-4 TEAEs, 16 (57.1%) patients experienced Grade 3-4 TRAEs.
- No patients experienced Grade 5 TEAEs.
- No patients discontinued treatment or died due to treatment related AEs.

Additional Grade 3-4 TRAEs(≥5%):

- Pneumonia (10.7%)
- Platelet count decreased (7.1%)

TRAE, treatment related adverse event.

**Data cut-off: April 12, 2021**

# Conclusions

- Pralsetinib showed broad and durable anti-tumor activity in Chinese patients with advanced or metastatic RET-mutant MTC, consistent with the data previously reported in the global ARROW study.
  - 73.1 % ORR and response observed regardless of RET mutation genotype
  - 9-month DOR rate was 100%, median DOR not reached
- Safety profile of pralsetinib in Chinese patients was manageable, no new safety signals detected.
- Pralsetinib may provide a potent targeted treatment for Chinese MTC patients with RET mutation.
- NDA currently under review by National Medical Products Administration (NMPA).

Data cut-off: April 12, 2021

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