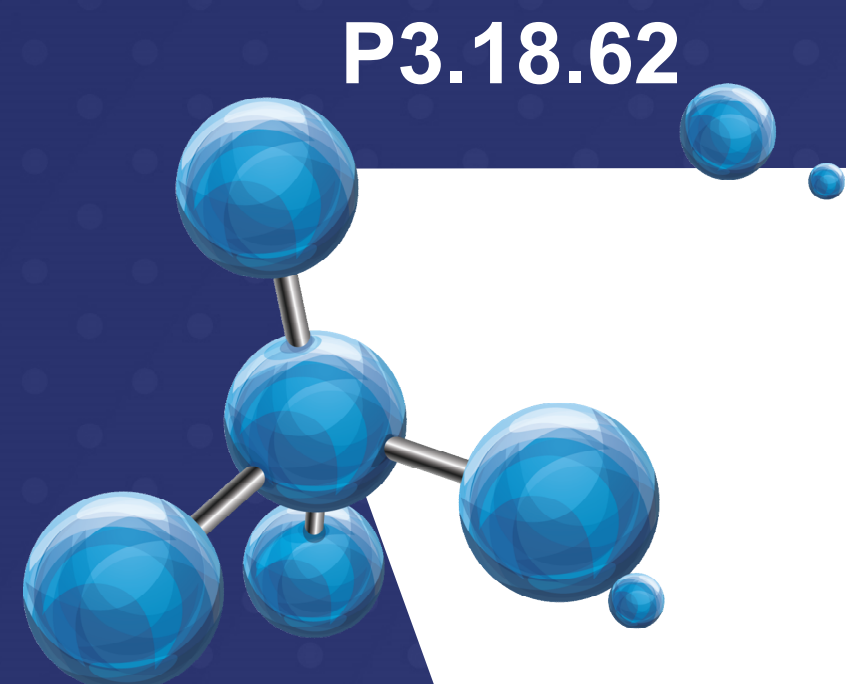




TRUST-III: Phase 3 Head-to-Head Study of Taletrectinib vs Crizotinib in Patients With ROS1+ Non-Small Cell Lung Cancer (NCT06564324)

Caicun Zhou,¹ Shengxiang Ren,² Linlin Wang,³ Jun Zhao,⁴ Yun Zhao,⁵ Huijie Fan,⁶ Bo Jin,⁷ Qian Chu,⁸ Feiwu Ran,⁹ Chang Su⁹

¹Department of Medical Oncology, Shanghai East Hospital and Thoracic Cancer Institute, Tongji University School of Medicine, Shanghai, China; ²Department of Medical Oncology, Shanghai Pulmonary Hospital, School of Medicine, Tongji University, Shanghai, China; ³Department of Radiation Oncology, Cancer Hospital of Shandong First Medical University, Jinan, China; ⁴Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department I of Thoracic Oncology, Peking University Cancer Hospital and Institute, Beijing, China; ⁵Department of Respiratory Oncology, Affiliated Tumor Hospital of Guangxi Medical University, Nanning, China; ⁶Department of Oncology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; ⁷Department of Medical Oncology, The First Affiliated Hospital of China Medical University, Shenyang, China; ⁸Department of Thoracic Oncology, Tongji Hospital Affiliated to Tongji Medical College of HUST, Wuhan, China; ⁹Nuvation Bio, New York, NY, USA



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Abbreviations

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; BIRC, Blinded Independent Review Committee; c, confirmed; CNS, central nervous system; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDA, Food and Drug Administration; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IC, intracranial; ILD, interstitial lung disease; NMPA, National Medical Products Administration; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; QD, once daily; R, randomized; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; ROS1, ROS proto-oncogene 1; SOC, standard of care; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor; TTP, time to disease progression; TTR, time to response; US, United States

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- IBTROZI™ (taletrectinib). Prescribing Information 2025

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Background & Rationale

- ROS1 gene fusions are oncogenic alterations occurring in approximately 2% of patients with NSCLC^{1,2}
- Patients with ROS1+ NSCLC are typically younger (median age of 50 years at diagnosis), never-smokers, female, diagnosed at an advanced stage, and with adenocarcinoma histology^{3,4}
- ROS1 TKIs are the current SOC for ROS1+ NSCLC¹
- Crizotinib was the first TKI approved for ROS1+ NSCLC but its utility is limited by poor CNS penetration and the development of resistance mutations, such as G2032R¹
- Taletrectinib is a next-generation, CNS-active, selective, oral ROS1 inhibitor with efficacy against the G2032R resistance mutation^{2,5}
- In a pooled analysis of two Phase 2 studies, TRUST-I and TRUST-II, taletrectinib demonstrated promising efficacy, including IC activity, and a favorable safety profile in patients with TKI-naïve and TKI-pretreated ROS1+ NSCLC⁵

Pooled Data From TRUST-I and TRUST-II⁵

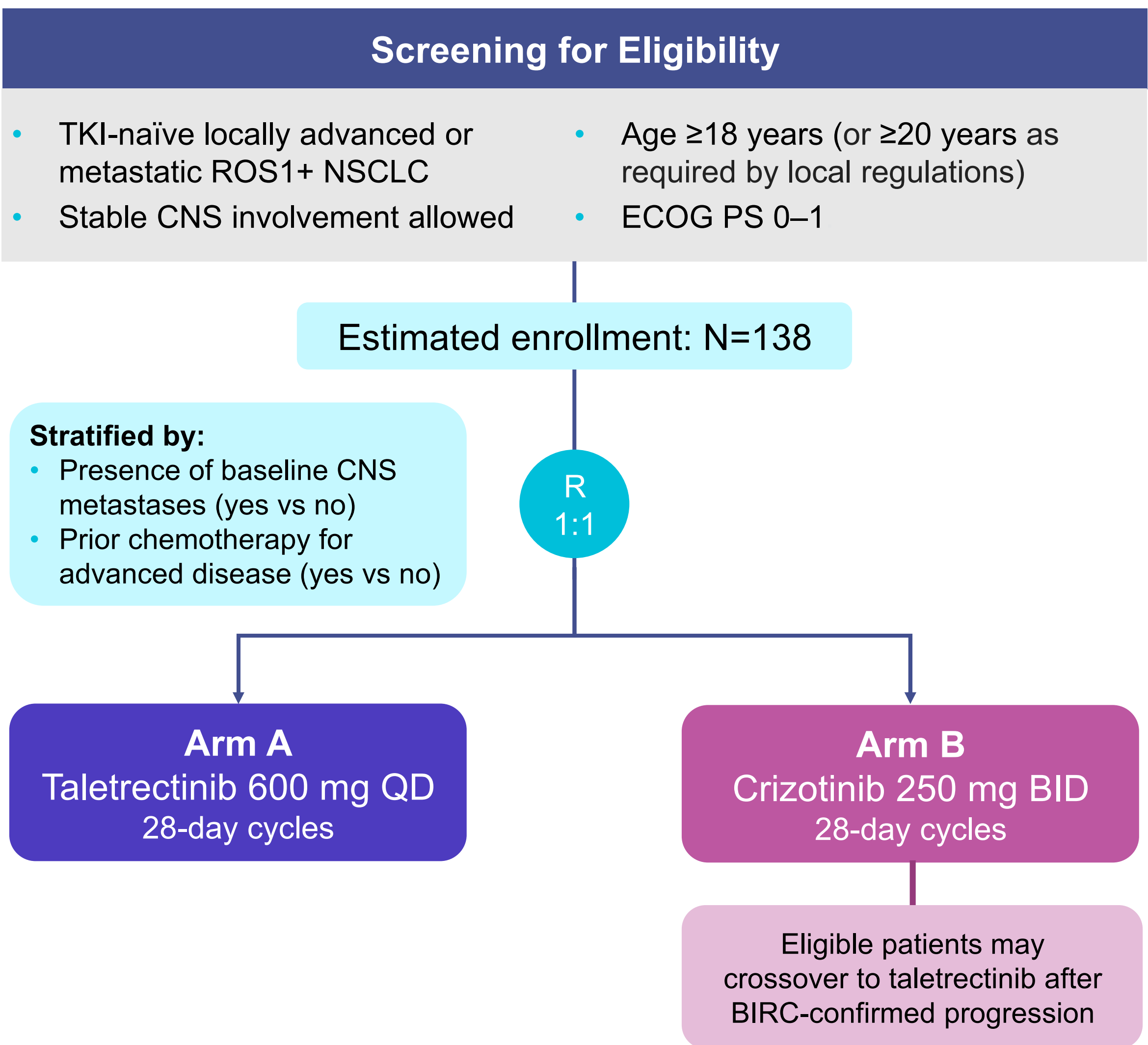
Efficacy	TKI-naïve (n=160)	TKI-pretreated (n=113)
cORR, %	88.8	55.8
Median DOR, months	44.2	16.6
Median PFS, months	45.6	9.7
IC Efficacy	(n=17)	(n=32)
IC-ORR, %	76.5	65.6

- The most common TEAEs with taletrectinib were elevated AST (72%), elevated ALT (68%), diarrhea (64%), nausea (46%), and vomiting (44%), most of which were Grade 1 or 2 in severity⁵
- Taletrectinib was approved by China's NMPA in January 2025 and by the US FDA in June 2025 for the treatment of adult patients with locally advanced or metastatic ROS1+ NSCLC^{6,7}
- This Phase 3 TRUST-III study aims to confirm the clinical benefit of taletrectinib compared with crizotinib in patients with ROS1+ NSCLC who have not previously received ROS1 TKIs
- This study is being conducted as part of a regulatory commitment to the NMPA, to support taletrectinib approval in China



TRUST-III Study Design

- TRUST-III (NCT06564324) is a Phase 3, open-label, multicenter, randomized study evaluating the efficacy and safety of taletrectinib vs crizotinib in TKI-naïve patients with locally advanced or metastatic ROS1+ NSCLC



Key Endpoints

Primary
PFS assessed by BIRC per RECIST v1.1
Secondary
cORR, DOR, TTR, and DCR assessed by BIRC and Investigator per RECIST v1.1
PFS assessed by Investigator per RECIST v1.1
IC endpoints assessed by BIRC per RECIST v1.1 (IC-ORR, IC-TTP, IC-DOR, IC-PFS)
Overall survival
Safety and tolerability
Pharmacokinetics
Patient-reported outcomes



Key Eligibility Criteria

Inclusion Criteria

- Histologically or cytologically confirmed locally advanced or metastatic ROS1+ NSCLC
- ≥1 measurable lesion(s) per Investigator assessment using RECIST v1.1
- Prior CNS metastases allowed if asymptomatic and stable (including leptomeningeal metastases)
- Age ≥18 years (or ≥20 years as required by local regulations)
- ECOG PS 0–1
- Adequate organ function

Exclusion Criteria

- Prior ROS1 TKIs
- Prior immune checkpoint inhibitors or ≥1 prior regimen(s) of systemic anticancer therapy
- Chemotherapy or radiation therapy ≤14 days prior to randomization
- Major surgery ≤28 days prior to randomization
- History or evidence of ILD or drug-related pneumonitis
- Active infection, including HBV, HCV, and HIV



Trial Progress

- TRUST-III (NCT06564324) is currently recruiting patients in China
- Estimated primary completion date: January 2029
- Estimated study completion date: September 2030

Summary

- Taletrectinib demonstrated high and durable response rates, along with a favorable safety profile, in patients with advanced or metastatic ROS1+ NSCLC,⁵ and is now approved in both China and the US^{6,7}
- TRUST-III (NCT06564324) is a Phase 3 study evaluating the efficacy and safety of taletrectinib vs crizotinib in TKI-naïve patients with locally advanced or metastatic ROS1+ NSCLC
- The primary endpoint is PFS, while secondary endpoints include ORR, DOR, IC efficacy, overall survival, and safety
- The study is currently recruiting patients in China with an estimated completion date of September 2030