

A Global Phase 2 Study of Taletrectinib, a Next-Generation of ROS1 TKI, in ROS1 Positive Lung Cancer and Other Solid Tumors (TRUST-II)



M. Nagasaka¹, S. Sugawara², C.-M. Choi³, T. Okamoto⁴, N. Yanagitani⁵, K. Nosaki⁶, T. Takahashi⁷, Y. Fujiwara⁸, H. Hayashi⁹, J. Khoury¹⁰, J. Nieva¹¹, A. Gabayan¹², L. Raez¹³, H. Chen¹⁴, A. Dimou¹⁵, N. Pennell¹⁶, G. Liu¹⁷, S.-H.I. Ou¹, T. Seto⁴, Y. Ohe¹⁸
1. University of California Irvine School of Medicine and Chao Family Comprehensive Cancer Center, Orange, CA, United States of America, 2. Sendai Kosei Hospital, Miyagi, Japan, 3. Asan Medical Center, Seoul, Korea, Republic of, 4. NHO Kyushu Cancer Center, Fukuoka, Japan, 5. The Cancer Institute Hospital of JFCR, Tokyo, Japan, 6. National Cancer Center Hospital East, Chiba, Japan, 7. Shizuoka Cancer Center, Shizuoka, Japan, 8. Aichi Cancer Center Hospital, Nagoya, Japan, 9. Kindai University Hospital, Osaka-sayama, Japan, 10. The oncology institute of hope and innovation, Whittier, CA, United States of America, 11. University of Southern California Keck School of Medicine, Los Angeles, CA, United States of America, 12. Beverly Hills Cancer Center, Los Angeles, CA, United States of America, 13. Memorial Cancer Institute/ Florida Atlantic University (FAU), Miami, FL, United States of America, 14. Roswell Park Comprehensive Cancer Center, Buffalo, NY, United States of America, 15. Mayo Clinic, Rochester, MN, United States of America, 16. Cleveland Clinic, Cleveland, OH, United States of America, 17. Princess Margaret Cancer Centre, Toronto, ON, Canada, 18. National Cancer Center Hospital, Tokyo, Japan

Background

- Non-small cell lung cancer (NSCLC) is by far one of the leading causes of cancer-related mortality globally. C-ros oncogene 1 (ROS1) rearrangements define a distinct molecular subtype of NSCLC and have been validated as an actionable therapeutic target.
- Taletrectinib (AB-106/DS-6051b), a brain-penetrant, highly potent and selective ROS1 tyrosine kinase inhibitor (TKI), has shown clinically meaningful efficacy and safety profiles in ROS1+ NSCLC patients in phase 1 studies in the U.S. and Japan^{1, 2} as well as in the ongoing phase 2 TRUST study (NCT04395677) in China^{3, 4}.
- Taletrectinib has notably demonstrated clinical activity against ROS1 G2032R resistance mutation and intracranial activity against central nervous system (CNS) metastases in the ongoing phase 2 TRUST study (NCT04395677) in China^{3, 4}.

Key study objectives

Primary Objective

- To evaluate the efficacy of taletrectinib by the objective response rate (ORR) in the patients with advanced or metastatic ROS1 positive NSCLC.

Secondary Objectives

- To evaluate the efficacy by the Duration of response (DOR); Progression-free survival (PFS); time to failure (TTF); time to response (TTR); Overall survival (OS); Intracranial activity
- To assess the safety and tolerability
- To determine pharmacokinetic profile.

Key inclusion criteria

- Histologically or cytologically confirmed locally advanced or metastatic tumors.
- Evidence of ROS1 fusion-positive tumor.
- At least one measurable disease per RECIST 1.1.
- ECOG Performance Status: 0 or 1.
- Adequate organ function.

Key exclusion criteria

Exclusion criteria

- Patient received other treatments prior to enrollment including investigational agents or anticancer therapy within 2 weeks, immuno-oncology within 12 weeks, and major surgery within 4 weeks.
- Radiation therapy with a limited field for palliation within 1 week before treatment.
- Unsolved adverse events caused by previous treatments.
- Use of food or drugs disrupting cytochrome P450 3A4/5 or p-glycoproteins.
- Administration of agents with potential QT interval prolonging effect.
- Tumor and/or cancerous meningitis caused spinal cord compression.
- Any gastrointestinal disorders that may affect absorption of oral medications.

Study design

This is a Phase 2, multi-country, multi-center, open-label, non-randomized study.

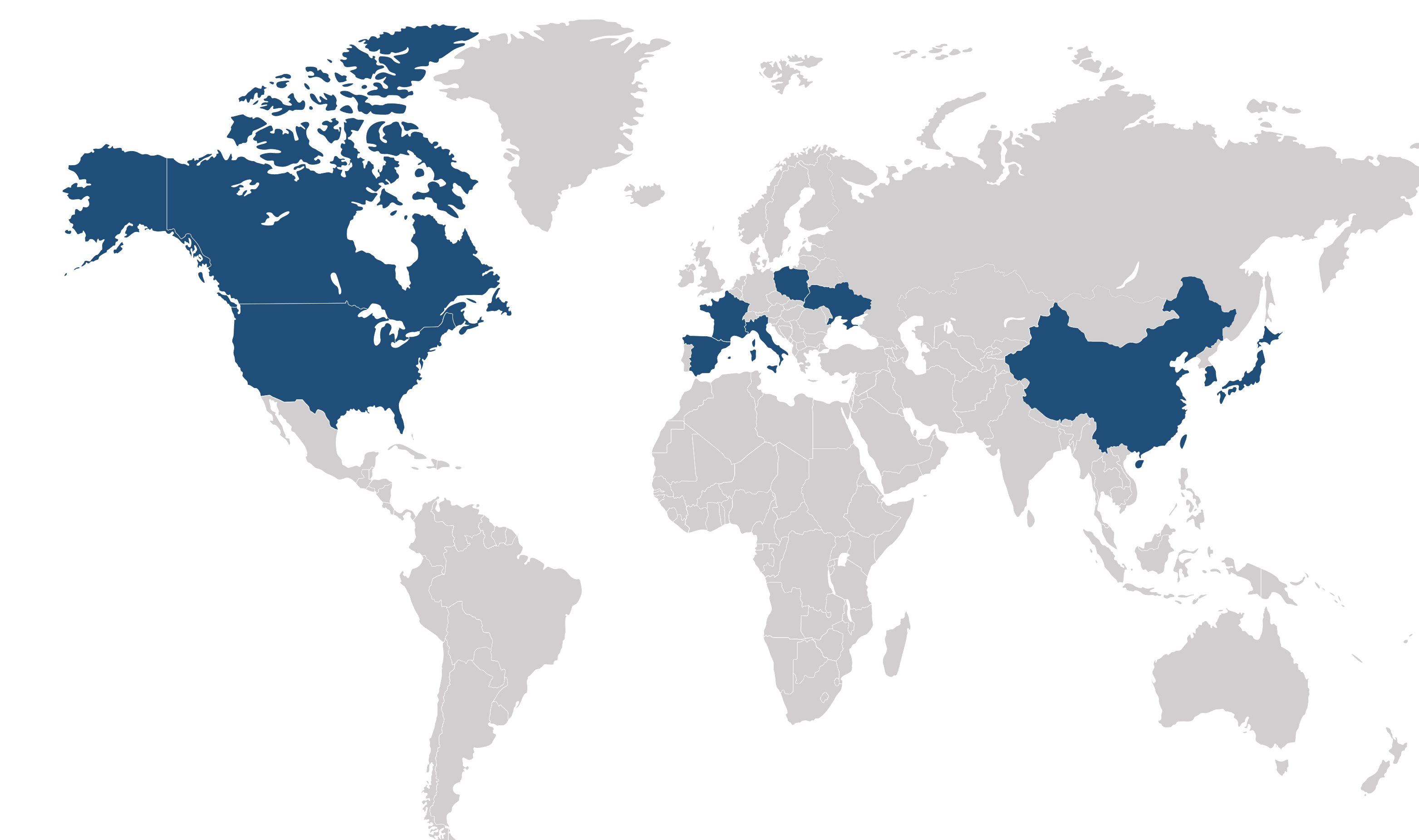
Treatment

- Taletrectinib 600 mg (3 capsules) once daily administered until disease progression and unacceptable toxicity

Cohorts

- **1.** systematic chemotherapy naïve or ≤ one prior line and ROS1 naïve NSCLC (N=53).
- **2.** one ROS1 TKI treatment and with progression, chemotherapy naïve or ≤ one line of platinum and/or pemetrexed based therapy, NSCLC (N=46).
- **3:** ≤2 prior ROS1 TKI treatments and with progression, either chemotherapy naïve or ≤2 lines of platinum and/or pemetrexed based therapy, NSCLC (N=10).
- **4:** ROS1 positive solid tumors other than NSCLC, naïve to systemic chemotherapy or ≤ 2 prior lines of chemotherapy, naïve to ROS1 TKI treatment (N=10).

Map of enrolling countries



Europe: France, Spain, Italy, Ukraine, Poland

Asia: China, Japan, South Korea

North America: United States of America, Canada

Trial information

Clinicaltrials.gov identifier: NCT04919811

Protocol number: AB-106-G208

Status: Recruiting

References

1. Fujiwara, et al., *Oncotarget* 2018; 9(34): 23729-23737
2. Ou, et al., *JTO Clin Res Rep.* 2020 Oct 21;2(1):100108
3. Zhou, et al., *ASCO Annual Meeting*, 2021
4. Zhou, et al., *CSCO Annual Meeting*, 2021

Acknowledgment

The study is sponsored by AnHeart Therapeutics, Inc.

Contact

For more information, please contact Dr. Misako Nagasaka
nagasakm@hs.uci.edu.