

October 2, 2026

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New Drug Application Submission Initiated for Zipalertinib Plus Chemotherapy in First-Line EGFR Exon 20 Insertion Mutation NSCLC for Review Under FDA Real-Time Oncology Review Program

Taiho Pharmaceutical Co., Ltd., announced on October 1 (U.S. time) the initiation of a New Drug Application (NDA) submission to the U.S. Food and Drug Administration (FDA) for zipalertinib in combination with platinum-based chemotherapy for the treatment of patients with previously untreated, locally advanced or metastatic non-small cell lung cancer (NSCLC) harboring epidermal growth factor receptor (EGFR) exon 20 insertion (ex20ins) mutations under the FDA's Real-Time Oncology Review (RTOR) program. The Company regards zipalertinib as one of its key future growth drivers and believes that this development represents an important milestone toward enhancing its medium- to long-term corporate value. There is no change to the Company's consolidated earnings forecast for the fiscal year ending December 31, 2026 at this time. The Company will promptly disclose any matters that should arise and require disclosure in the future.

The RTOR program allows sponsors to submit clinical data in advance of the complete application to facilitate earlier review of efficacy and safety results. Completion of the NDA submission is expected by year-end 2026.

The NDA submission is based on data from the Phase 3 REZILIENT3 trial, which met its primary endpoint in the planned interim analysis, demonstrating a statistically significant and clinically meaningful improvement in progression-free survival for zipalertinib plus chemotherapy compared to chemotherapy alone.

About Zipalertinib

Zipalertinib (development code: CLN-081/TAS6417) is an orally available small molecule designed to target activating mutations in EGFR. The molecule was selected because of its ability to inhibit EGFR variants with exon 20 insertion mutations. Zipalertinib is designed as a next generation, irreversible EGFR inhibitor for the treatment of a genetically defined subset of patients with non-small cell lung cancer. NDA for zipalertinib monotherapy in patients with locally advanced or metastatic EGFR ex20ins

mutation NSCLC who have previously received platinum-based chemotherapy remains under FDA review, with a Prescription Drug User Fee Act (PDUFA) target action date of February 27, 2027. Zipalertinib is investigational and has not been approved by any health authority.

Zipalertinib is being developed by Taiho Oncology, Inc., its parent company, Taiho Pharmaceutical Co., Ltd., and in collaboration with Cullinan Therapeutics, Inc. in the U.S.

About EGFR Exon 20 Insertion Mutations

NSCLC is a common form of lung cancer and up to 4% of all cases globally have EGFR ex20ins.¹ In the United States, approximately 16% of patients with NSCLC harbor EGFR mutations,¹ with insertions at exon 20 accounting for up to 12% of these mutations.²

1. Burnett H, Emich H, Carroll C, et al. Epidemiological and clinical burden of EGFR exon 20 insertion in advanced non-small cell lung cancer: a systematic literature review. PLOS ONE. 2021;16(3): e0247620. Available at: <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0247620>.
2. Riess JW, Gandara DR, Frampton GM, et al. Diverse EGFR Exon 20 Insertions and Co-Occurring Molecular Alterations Identified by Comprehensive Genomic Profiling of NSCLC. Journal of Thoracic Oncology. 2018 Jul 5;13(10):1560–1568. Available at: [https://www.jto.org/article/S1556-0864\(18\)30770-6/pdf](https://www.jto.org/article/S1556-0864(18)30770-6/pdf).