TPS8650 **Poster Session**

Phase 1/2 clinical trial of JIN-A02, a 4th generation EGFR-TKI in EGFR-mutated advanced/metastatic non-small cell lung cancer.

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Background: Epidermal growth factor receptor (*EGFR*) mutations are the predominant drivers of NSCLC. While EGFR tyrosine kinase inhibitors (TKIs) are the primary treatment for *EGFR*-mutant NSCLC patients, resistance inevitably develops, leading to disease progression. JIN-A02, a novel 4th generation EGFR-TKI, intended for oral administration, selectively and reversibly binds to *EGFR* mutations, including the C797S and/or T790M mutation that causes resistance to 3rd generation of EGFR-TKIs. Preclinical studies with *EGFR* C797S and/or T790M mutated cell lines and C797S+ xenograft mice model showed that JIN-A02 inhibits cell and tumor growth in a dose dependent manner and exhibits high selectivity over wild-type *EGFR*. Moreover, JIN-A02 has been shown to penetrate the blood-brain barrier and exhibit anti-tumor activity in an intracranial tumor model. This phase 1/2 study is designed to evaluate the safety and anti-tumor activity of JIN-A02 in *EGFR*-mutant NSCLC patients. **Methods:** JIN-A02 is under evaluation in Phase 1/2, multicenter, an open-label trial (NCT05394831) for subjects with advanced NSCLC harboring C797S and/or T790M mutation as a monotherapy. The primary objective is to assess safety, tolerability, pharmacokinetics, and anti-tumor effect for determining the recommended phase 2 dose (RP2D) of JIN-A02. Inclusion criteria are that the subject ($\geq$ 18 years) must have advanced or metastatic NSCLC showing progressive disease post-treatment with approved standard EGFR-TKIs and/or platinum-based anticancer chemotherapy, with ECOG status 0 or 1. The study consists of 3 parts: dose escalation (Part A), dose exploration (Part B), and dose expansion (Part C). In Part A, JIN-A02 is administered orally once daily from 12.5 mg, and at least 3 subjects are recruited per cohort conducted over 28 days cycles to evaluate the maximum tolerated dose. Dose escalation between cohorts is made at up to twice the prior dose level. Dose-limiting toxicities (DLTs) are assessed over 21 days. Part B aims to further evaluate JIN-A02 safety to determine the RP2D using two preliminary effective dose levels from Part A. In Part C, subjects are divided into 5 cohorts based on the EGFR mutation status (both or single positive for C797S and T790M), and the anti-tumor activity of JIN-A02 is evaluated according to RECIST v1.1 at the RP2D. Clinical trial information: NCT05394831. Research Sponsor: None.