IMS-P18 **Pharmacological Evaluation of ASP8273, a Mutant-Selective Irreversible EGFR Inhibitor for EGFR Activating Mutations and T790M Resistance Mutation**

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Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors have shown antitumor efficacy for non-small cell lung cancer (NSCLC) patients with EGFR activating mutations positive tumors. However, the clinical efficacy of these agents is limited by the development of acquired drug resistance, which is most commonly caused by T790M mutation in EGFR. ASP8273 inhibited mutant EGFR containing deletion in exon 19 (del ex19) or L858R activating mutations as well as T790M resistance mutation with lower IC_{50} values than wild type EGFR in vitro. Mass spectrometry analysis revealed that ASP8273 is covalently bound to a mutant EGFR via C797 in the kinase domain. In murine xenograft studies, ASP8273 induced tumor regression in HCC827, PC-9 (del ex19) and NCI-H1975 (L858R/T790M) xenograft models without body weight loss. These results suggest therapeutic potential of ASP8273 in NSCLC patients with tumors harboring EGFR mutations.