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A Structure-Guided Optimization of Pyrido[2,3-*d*]pyrimidin-7-ones as Selective Inhibitors of EGFR$^{L858R/T790M}$ Mutant with Improved Pharmacokinetic Properties

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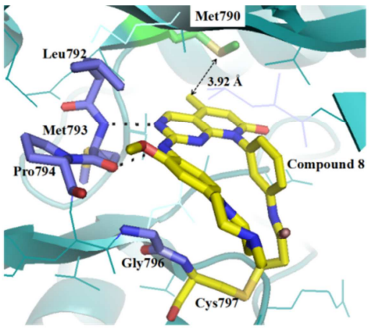

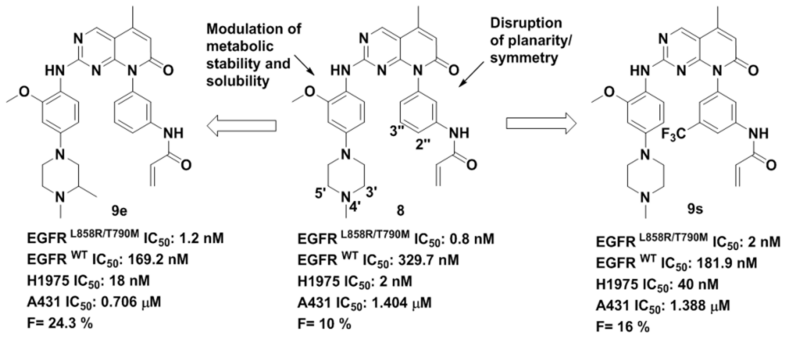

Structural optimization of pyrido[2,3-*d*]pyrimidin-7-ones yielded new selective EGFR^{T790M} inhibitors. Compound **9s** exhibited good pharmacokinetic properties with F value of 16%, and inhibited EGFR$^{L858R/T790M}$ kinase and H1975 cells with IC_{50} values of 2.0 and 40 nM, respectively.