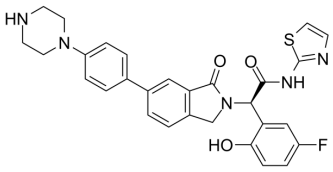
JBJ-04-125-02

Cat. No.:	HY-135805
CAS No.:	2060610-53-7
Molecular Formula:	$C_{29}H_{26}FN_5O_3S$
Molecular Weight:	543.61
Target:	EGFR
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

JBJ-04-125-02 is a potent, mutant-selective, allosteric and orally active EGFR inhibitor with an IC_{50} of 0.26 nM for EGFR $^{L858R/T790M}$. JBJ-04-125-02 can inhibit cancer cell proliferation and EGFR$^{L858R/T790M/C797S}$ signaling. JBJ-04-125-02 has anti-tumor activities[1].

IC_{50} & Target

EGFR (L858R/T790M)
0.26 nM (IC_{50})

In Vitro

JBJ-04-125-02 (0-1000 nM; 72 hours; H1975 cells) treatment could inhibit cell proliferation of H1975 cells at low nanomolar concentrations[1].
JBJ-04-125-02 treatment also inhibits cell proliferation in Ba/F3 cells stably transfected with EGFR^{L858R}, EGFR$^{L858R/T790M}$, or EGFR$^{L858R/T790M/C797S}$ mutations[1].
The ability of JBJ-04-125-02 (0.01-10 μM) to inhibit EGFR phosphorylation using Ba/F3, H1975 and NIH-3T3 cells is examined. JBJ-04-125-02 demonstrates mutant selectivity by inhibiting mutant EGFR and downstream AKT and ERK1/2 phosphorylation[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	H1975 cells
Concentration:	0 nM, 0.1 nM, 1 nM, 10 nM, 100 nM, 1000 nM
Incubation Time:	72 hours
Result:	Inhibited cell proliferation of H1975 cells at low nanomolar concentrations.

In Vivo

JBJ-04-125-02 (50 mg/kg; oral gavage; once daily; for 15 weeks; EGFR$^{L858R/T790M/C797S}$ genetically engineered mice) treatment leads to marked tumor regressions within 4 weeks of treatment[1].
JBJ-04-125-02 exhibits a moderate half-life of 3 hours and a high area under curve of 728,577 min•ng/mL (AUClast) following 3 mg/kg intravenous (i.v.) dose. A 20 mg/kg oral dose of JBJ-04-125-02 achieves an average maximal plasma concentration of 1.1 μmol/L with an oral bioavailability of 3%[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	$EGFR^{L858R/T790M/C797S}$ genetically engineered mice (GEM)[1]
Dosage:	50 mg/kg
Administration:	Oral gavage; once daily; for 15 weeks
Result:	Led to marked tumor regressions within 4 weeks of treatment.

REFERENCES

[1]. To C, et al. Single and Dual Targeting of Mutant EGFR with an Allosteric Inhibitor. Cancer Discov. 2019 Jul;9(7):926-943.

Caution: Product has not been fully validated for medical applications. For research use only.

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