JBJ-09-063 TFA

Cat. No.: HY-147183A

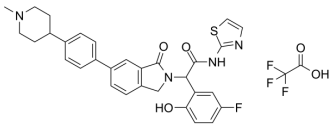
Molecular Formula: $C_{33}H_{30}F_4N_4O_5S$

Molecular Weight: 670.67

Target: EGFR

Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (149.10 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.4910 mL	7.4552 mL	14.9105 mL
5 mM	0.2982 mL	1.4910 mL	2.9821 mL
10 mM	0.1491 mL	0.7455 mL	1.4910 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

JBJ-09-063 TFA is a mutant-selective allosteric EGFR inhibitor with IC_{50}s of 0.147 nM, 0.063 nM, 0.083 nM and 0.396 nM for EGFR L858R, EGFR L858R/T790M, EGFR L858R/T790M/C797S and EGFRLT/L747S. JBJ-09-063 TFA effectively reduces EGFR, Akt and ERK1/2 phosphorylation. JBJ-09-063 TFA is effective across EGFR tyrosine kinase inhibitor (TKI)-sensitive and resistant models. JBJ-09-063 TFA can be used for researching EGFR-mutant lung cancer[1].

IC_{50} & Target

EGFR L858R	EGFR L858R/T790M	EGFR L858R/T790M/C797S	EGFRLT/L747S
0.147 nM (IC_{50})	0.063 nM (IC_{50})	0.083 nM (IC_{50})	0.396 nM (IC_{50})

In Vitro

JBJ-09-063 is remarkably effective at inhibiting cell growth and leads to a significant increase in apoptosis, even though H3255GR cells are resistant to gefitinib as a single agent, as they contain an EGFR T790M mutation[1].
JBJ-09-063 is effective in H1975 cells exogenously expressing the osimertinib-resistant mutations[1].
JBJ-09-063 exhibits IC_{50}s of 50 nM and 6 nM in Ba/F3 cell when use alone or combination with Cetuximab (HY-P9905)[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

JBJ-09-063 (3 mg/kg i.v., 20 mg/kg p.o.) exhibits favorable pharmacokinetics properties and is sufficiently stable to deliver good efficacy upon oral dosing[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Mice[2]
Dosage:	3 mg/kg for i.v., 20 mg/kg for p.o.
Administration:	i.v. and p.o.; single dosage
Result:	Pharmacokinetic Parameters of JBJ-09-063 in mice[2].

Cl (mL/min/kg), i.v.	$T_{1/2}$ (h)	V_{ss} (L/kg)	F (%)	AUC 8h (ng·h/mL)
15.7	2.3	2.5	15	2398

REFERENCES

[1]. To C, et al. An allosteric inhibitor against the therapy-resistant mutant forms of EGFR in non-small cell lung cancer. Nat Cancer. 2022 Apr;3(4):402-417.

[2]. Gero TW, Scott DA, et al. Quinazolinones as allosteric fourth-generation EGFR inhibitors for the treatment of NSCLC. Bioorg Med Chem Lett. 2022 Jul 15;68:128718.

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