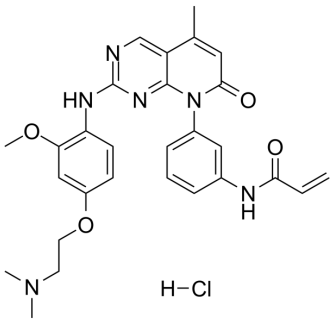
EGFR-IN-1 hydrochloride

Cat. No.:	HY-19617A
CAS No.:	2227455-78-7
Molecular Formula:	$C_{28}H_{31}ClN_6O_4$
Molecular Weight:	551.04
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	EGFR-IN-1 hydrochloride is an orally active and irreversible L858R/T790M mutant selective EGFR inhibitor. EGFR-IN-1 hydrochloride potently inhibits Gefitinib-resistant EGFR L858R, T790M with 100-fold selectivity over wild-type EGFR. EGFR-IN-1 hydrochloride displays strong antiproliferative activity against the H1975 cells and the first line mutant HCC827 cells. Antitumor activity[1].
IC_{50} & Target	$EGFR^{L858R/T790M}$

In Vitro

EGFR-IN-1 hydrochloride (compound 24) (10 μM; 72 hours) displays strong antiproliferative activity against the H1975 and HCC827 cells with IC50s of 4 and 28 nM, respectively[1].

EGFR-IN-1 hydrochloride inhibits p-EGFR in H1975 and HCC827 cells with IC_{50}s of 4 and 9 nM, respectively. EGFR-IN-1 highly selective against a panel of 100 kinases[1].

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

Cell Proliferation Assay[1]

Cell Line:	NSCLC cell lines H1975 (T790M/L858R), HCC827 (Δ746-750)
Concentration:	10 μM
Incubation Time:	72 hours
Result:	Inhibited H1975 nonsmall cell lung cancer cell line and the first line mutant HCC827 cell line with IC_{50}s of 4 and 28 nM, respectively.

In Vivo

EGFR-IN-1 hydrochloride (30 mg/kg; p.o.; daily for 2 weeks) displays significant tumor growth inhibition with no observed loss in body weight[1].

EGFR-IN-1 hydrochloride evaluates in a time course PD experiment upon oral dosing at 30 mg/kg. EGFR-IN-1 shows a >50% inhibition of phosphorylation of EGFR for >12 h. EGFR-IN-1 reaches maximal concentration of 0.10 μM at 2 h and systemic exposure (AUC0-inf.) is 0.33 μM. h[1].

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Animal Model:	Female athymic nude mice (H1975 Tumor Xenograft)[1]

Dosage:	30 mg/kg
Administration:	p.o.; daily for 2 weeks
Result:	Led to significant tumor growth inhibition with no observed loss in body weight.

REFERENCES

[1]. Wurz RP, et al. Oxopyrido[2,3-d]pyrimidines as Covalent L858R/T790M Mutant Selective Epidermal Growth Factor Receptor (EGFR) Inhibitors. ACS Med Chem Lett. 2015 Jul 27;6(9):987-92.

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