FIIN-3

Cat. No.: HY-18603

CAS No.: 1637735-84-2

Molecular Formula: $C_{34}H_{36}Cl_2N_8O_4$

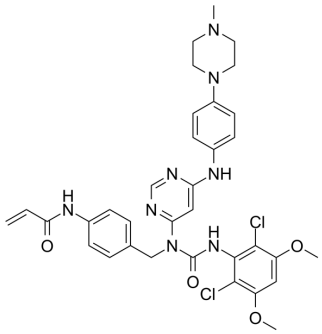
Molecular Weight: 691.61

Target: EGFR; FGFR

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

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 10 mg/mL (14.46 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4459 mL	7.2295 mL	14.4590 mL
	5 mM	0.2892 mL	1.4459 mL	2.8918 mL
	10 mM	0.1446 mL	0.7230 mL	1.4459 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (3.61 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.61 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.61 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

FIIN-3 is an irreversible inhibitor of FGFR with an IC_{50} of 13.1, 21, 31.4, and 35.3 nM for FGFR1, FGFR2, FGFR3 and FGFR4, respectively.

IC_{50} & Target

FGFR1	FGFR2	FGFR3	FGFR4
13.1 nM (IC_{50})	21 nM (IC_{50})	31.4 nM (IC_{50})	35.3 nM (IC_{50})

In Vitro

FIIN-3 potently inhibits both WT FGFRs (EC_{50} in the 1- to 41-nM range) and the gatekeeper mutant of FGFR2 (EC_{50} of 64 nM).

FIIN-3 also strongly inhibits EGFR, with an EC_{50} of 43 nM. FIIN-3 shows good potency against gatekeeper mutant V564F; FIIN-3 also is potent against the gatekeeper-plus-1 mutant E565K; FIIN-3 also displays antiproliferative activity (with an EC_{50} of 135 nM) against Ba/F3 cells transformed by the EGFR vIII fusion protein, which has a WT EGFR kinase domain. FIIN-3 shows even better activity against EGFR mutant L858R (EC_{50} of 17 nM) and moderate activity, displaying an EC_{50} of 231 nM, against the EGFR mutant L858R/T790M mutant. In WT FGFR2 Ba/F3 cells, FIIN-3 completely inhibits the FGFR2 autophosphorylation on Tyr656/657 at concentrations as low as 3 nM. In FGFR2 V564M Ba/F3 cells, FIIN-3 is capable of inhibiting the FGFR2 mutant V564M autophosphorylation with partial inhibition at 100 nM and complete inhibition observed at 300 nM[1].

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

PROTOCOL

Cell Assay [1]

TEL-FGFR2–transformed Ba/F3 cells are seeded in a 96-well plate and are treated with each concentration of FIIN-3. After 72 h the cells are assessed by MTS tetrazolium assay[1].

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

REFERENCES

[1]. Tan L et al. Development of covalent inhibitors that can overcome resistance to first-generation FGFR kinase inhibitors. Proc Natl Acad Sci U S A, 2014 Nov 11, 111(45):E4869-77

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