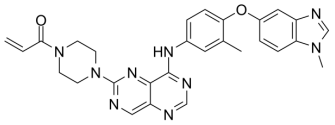
BI-4142

Cat. No.:	HY-150024
CAS No.:	2682003-36-5
Molecular Formula:	$C_{28}H_{27}N_9O_2$
Molecular Weight:	521.57
Target:	EGFR
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (191.73 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9173 mL	9.5864 mL	19.1729 mL
	5 mM	0.3835 mL	1.9173 mL	3.8346 mL
	10 mM	0.1917 mL	0.9586 mL	1.9173 mL

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

BIOLOGICAL ACTIVITY

Description

BI-4142 is a potent, highly selective and orally active HER2 inhibitor with an IC_{50} of 5 nM[1].

IC_{50} & Target

HER2
5 nM (IC_{50})

In Vitro

BI-4142 shows inhibition with IC_{50} values of 10 nM, 18 nM, 270 nM and 2400 nM against HEK $HER2^{YVMA}$, Ba/F3 $HER2^{YVMA}$, HEK $EGFR^{WT}$ and Ba/F3 $EGFR^{WT}$, respectively[1].
BI-4142 (1 nM-5 μM, 72 h or 96 h) shows antiproliferative activity against tumor cells[1].
BI-4142 displays good permeability and no PgP-mediated efflux liability in the CaCo-2 assay[1].
BI-4142 inhibits HER2-dependent cell lines and inhibits downstream signaling[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	NCI-H2170 $HER2^{WT}$, NCI-H2170 $HER2^{YVMA}$, A431 $EGFR^{WT}$, Ba/F3 $HER2^{YVMA}$, Ba/F3 $HER2^{YVMA,S783C}$, Ba/F3 $EGFR^{WT}$ and Ba/F3 $EGFR^{C775S}$ cells

Concentration:	1 nM-5 μM
Incubation Time:	72 h or 96 h
Result:	Showed antiproliferative effect with IC_{50} values of 16 nM, 82 nM, >5 μM, 4 nM, 24 nM, 718 nM and 43 nM against NCI-H2170 $HER2^{WT}$, NCI-H2170 $HER2^{YVMA}$, A431 $EGFR^{WT}$, Ba/F3 $HER2^{YVMA}$, Ba/F3 $HER2^{YVMA,S783C}$, Ba/F3 $EGFR^{WT}$ and Ba/F3 $EGFR^{C775S}$, respectively.

In Vivo

BI-4142 (0-100 mg/kg; p.o.; twice per day for 40 days) inhibits tumor growth and inhibits oncogenic signaling[1].

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

Animal Model:	NMRI-Foxn1nu mice, PC-9 $HER2^{YVMA}$ xenograft model[1]
Dosage:	3, 10, 30 and 100 mg/kg
Administration:	Oral administration, twice per day for 40 days
Result:	Resulted in tumor regressions in a dose-dependent manner (113%, 126%, 153% and 166% tumor growth inhibition at 3, 10, 30 and 100 mg/kg, respectively).

Animal Model:	BomTac:NMRI Foxn1nu mice[1]
Dosage:	1 mg/kg or 10mg/kg and 100 mg/kg
Administration:	IV for 1 mg/kg, PO for 10mg/kg and 100 mg/kg (Pharmacokinetic Analysis)
Result:	In vivo mouse PK data for BI-4142[1]

Compound	Dose iv/po (mg/kg)	tmax (h)	C_{max} (nM)	AUD (h•nM)	Plasma CL (mL/min/kg)	% F
	i.v., 1mg/kg	n/a	n/a	3,280	9.69	n/a
BI-4142	p.o., 10 mg/kg	0.83	8,600	23,200	n/a	71
	p.o., 100 mg/kg	0.67	36,400	196,000	n/a	60

REFERENCES

[1]. Wilding B, et al. Discovery of potent and selective HER2 inhibitors with efficacy against HER2 exon 20 insertion-driven tumors, which preserve wild-type EGFR signaling. Nat Cancer. 2022 Jul;3(7):821-836.

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