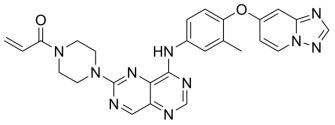
BI-1622

Cat. No.:	HY-150023
CAS No.:	2681392-19-6
Molecular Formula:	$C_{26}H_{24}N_{10}O_2$
Molecular Weight:	508.53
Target:	EGFR; Itk; PI4K; Btk; CDK; Raf; JAK
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; PI3K/Akt/mTOR; Cell Cycle/DNA Damage; MAPK/ERK Pathway; Epigenetics; Stem Cell/Wnt
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 (196.65 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9665 mL	9.8323 mL	19.6645 mL
	5 mM	0.3933 mL	1.9665 mL	3.9329 mL
	10 mM	0.1966 mL	0.9832 mL	1.9665 mL

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

BIOLOGICAL ACTIVITY

Description

BI-1622 is an orally active, potent and highly selective HER2 (ERBB2) inhibitor, with an IC_{50} of 7 nM. BI-1622 shows greater than 25-fold selectivity over EGFR. BI-1622 shows high antitumor efficacy in vivo in xenograft mouse tumor models with engineered H2170 and PC9 cells and had a favorable agent metabolism and pharmacokinetics profile[1].

IC_{50} & Target

HER2 7 nM (IC_{50})	ErbB4	EGFR	CDK11B
JAK3			

In Vitro

BI-1622 (0-5 μM, 72 h or 96 h) inhibits the proliferation of HER2-dependent cell lines[1].
BI-1622 induces a dose-dependent decrease in pHER2 and pERK levels in NCI-H2170 HER2YVMA and PC-9 HER2YVMA cells with an accompanying decrease in DUSP6 messenger RNA levels[1].
BI-1622 displays good permeability and no PgP-mediated efflux liability[1].
BI-1622 shows good in vitro clearance in mouse liver microsomes and mouse hepatocytes[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	Ba/F3 cells
Concentration:	0-5 μM
Incubation Time:	72 h or 96 h
Result:	Potently inhibited the proliferation of cancer cell lines dependent on amplified HER2 or an NRG-1 fusion. Inhibited different HER2 oncogenic variants and HER2WT with IC_{50} values below 50 nM in tumor cell lines, while sparing EGFRWT-driven cells.

In Vivo

BI-1622 (1 mg/kg, IV; 10 and 100 mg/kg, Orally; once) shows moderate clearance, a moderate volume of distribution, and good to moderate bioavailability[1].

BI-1622 (0-100 mg/kg, orally, twice daily) inhibits tumor growth and inhibits oncogenic signaling in vivo[1].

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

Animal Model:	Female NMRI-Foxn1nu mice (6-8 weeks old, 8-10 mice per cage, engrafted subcutaneously with PC-9 HER2YVMA, NCI-H2170 HER2YVMA or NCI-N87 cells)[1]
Dosage:	10, 30 and 100 mg/kg
Administration:	orally, twice daily
Result:	In the NCI-H2170 HER2YVMA mechanistic model, 100 mg/kg twice daily BI-1622 resulted in a delay in tumor growth (73% TGI). In the ST3107 HER2 exon 20 mutant model, both BI-4142 (100 mg/kg twice daily) resulted in tumor regressions.

Animal Model:	NMRI Foxn1nu mice (n=3 per group)[1]
Dosage:	1 mg/kg (IV); 10 and 100 mg/kg (Orally)
Administration:	IV, Orally; once (Pharmacokinetic Analysis)
Result:	Showed moderate in vivo clearance (50% hepatic blood flow), a moderate volume of distribution, and good to moderate bioavailability of up to 68%.

REFERENCES

[1]. Lamarre L, 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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