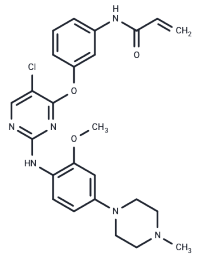
Data Sheet (Cat.No.T6238)

TargetMol

WZ4002

Chemical Properties



CAS No. : 1213269-23-8

Formula: C25H27ClN6O3

Molecular Weight: 494.97

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	WZ4002 is a mutant-selective EGFR inhibitor for EGFR(L858R) and EGFR(T790M) with IC50 of 2 nM/8 nM.
Targets(IC50)	EGFR
In vitro	WZ4002 inhibits other EGFR genotypes E746_A750 and E746_A750/T790M with IC50 of 2 and 6 nM. Besides, WZ4002 suppresses widetype ERBB2 with an IC50 of 32 nM. WZ4002 inhibits EGFR, AKT and ERK1/2 phosphorylation in NSCLC cell lines and WZ4002 prevents of EGFR phosphorylation in NIH-3T3 cells expressing different EGFR T790M mutant alleles. For WZ4002, kinases that exhibited greater than 95% inhibition relative to the DMSO control at 10 μM are selected for measurement of their dissociation constants. WZ4002, which possesses an ortho-methoxy group at the C2-aniline substituent, is more selective for EGFR compared to WZ3146. WZ4002 is 100-fold less effective at inhibiting phosphorylation of WT EGFR compared to the quinazoline inhibitors. Similarly, WZ4002 prevents EGFR kinase activity of recombinant L858R/T790M protein more potently than of WT EGFR, while the opposite is observed with HKI-272 and gefitinib. [1] In addition, the phosphorylated EGFR of Src TKI-resistant H1975 cells, as well as HCC827 cells, is completely suppressed by the third generation EGFR TKI, WZ4002. [2]
In vivo	In a 2-week efficacy study, WZ4002 treatment results in significant tumor regressions compared to vehicle alone in both T790M containing murine models. [1] Treatment with low-dose WZ4002, and high-dose WZ4002 leads to mean decreases in tracer uptake of 26%, and 36%, respectively. [3]
Kinase Assay	EGFR kinase assays: In vitro inhibitory enzyme kinetic assays using recombinant EGFR L858R/T790M and WT protein and are performed using the ATP/NADH coupled assay system in a 96-well format. WZ4002 is added to determine its inhibitory effects.
Cell Research	The NSCLC, Ba/F3 cells, NIH-3T3 cells, PC9 gR4 cells are used and verified to contain EGFR delE746_A750/T790M by direct sequencing. Cell proliferation and growth assays are performed using the MTS assay. Site directed mutagenesis is performed using the Quick Change Site-Directed Mutagenesis kit.(Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 11 mg/mL (22.22 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0203 mL	10.1016 mL	20.2032 mL
5 mM	0.4041 mL	2.0203 mL	4.0406 mL
10 mM	0.202 mL	1.0102 mL	2.0203 mL
50 mM	0.0404 mL	0.202 mL	0.4041 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Zhou W, et al. Nature. 2009, 462(7276), 1070-1074.
Jin X, Yang Y, Liu D, et al.Identification of a covalent NEK7 inhibitor to alleviate NLRP3 inflammasome-driven metainflammation.Cell Communication and Signaling.2024, 22(1): 565.
Sakuma Y, et al. Lab Invest. 2012, 92(3), 371-383.
Zannetti A, et al. J Nucl Med. 2012, 53(3), 443-450.