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Produktinformation

- Forschungsprodukte & Biochemikalien
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- Diagnostik & molekulare Diagnostik
- Laborgeräte & Service

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See the following pages for more information!

Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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WZ4002

Cat. No.: HY-12026

CAS No.: 1213269-23-8

Molecular Formula: $C_{25}H_{27}ClN_6O_3$

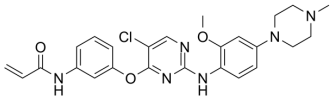
Molecular Weight: 495

Target: EGFR

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 (20.20 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0202 mL	10.1010 mL	20.2020 mL
	5 mM	0.4040 mL	2.0202 mL	4.0404 mL
	10 mM	0.2020 mL	1.0101 mL	2.0202 mL

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

BIOLOGICAL ACTIVITY

Description

WZ4002 is a mutant selective EGFR inhibitor with IC_{50}s of 2, 8, 3 and 2 nM for $EGFR^{L858R}$, $EGFR^{L858R/T790M}$, $EGFR^{E746\_A750}$ and $EGFR^{E746\_A750/T790M}$, respectively.

IC_{50} & Target

$EGFR^{L858R}$	$EGFR^{L858R/T790M}$	$EGFR^{E746\_A750}$	$EGFR^{E746\_A750/T790M}$
2 nM (IC_{50}, Cell Assay)	8 nM (IC_{50}, Cell Assay)	3 nM (IC_{50}, Cell Assay)	2 nM (IC_{50}, Cell Assay)

In Vitro

WZ4002 increases cellular potency correlated with inhibition of EGFR, AKT and ERK1/2 phosphorylation in NSCLC cell lines and EGFR phosphorylation in NIH-3T3 cells expressing different $EGFR^{T790M}$ mutant alleles. WZ4002 inhibits EGFR kinase activity of recombinant L858R/T790M protein more potently than of WT EGFR[1].

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

In Vivo

In a pharmacodynamic study WZ4002 effectively inhibits EGFR, AKT and ERK1/2 phosphorylation which is associated with a significant increase in TUNEL positive and a significant decrease in Ki67 positive cells compared to vehicle alone treated mice. In a 2 week efficacy study, WZ4002 treatment results in significant tumor regressions compared to vehicle alone in both T790M containing murine models. Histological evaluation of the lungs following treatment confirms significant

	resolution of the tumor nodules with only few small residual nodules and nodule remnants that has evidence of treatment effect with decreased cellularity and increased fibrosis consistent with remodeling/scarring[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	EGFR kinase assay is performed using a GST-kinase fusion protein. The final reaction mixture contained 60 mM HEPES pH 7.5, 5 mM $MgCl_2$, 5 mM $MnCl_2$, 3 mM Na_3V0_4, 1.25 mM DTT, 20 μM ATP, 1.5 μM PTP1B (Tyr66) biotinylated peptide and 50 ng of EGFR kinase. A phospotyrosine mab (pTyr100) is used to detect phosphorylation of the EGFR substrate peptide in the presence of WZ4002, gefitinib or HKI-272 (concentration ranges 0-10 μM for all drugs) followed a fluorescent Anti-mouse IgG secondary antibody. Fluorescence emission is detected at 615 nm[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Growth and inhibition of growth is assessed by MTS assay. Ba/F3 cells are exposed to WZ4002 treatment for 72 hours. Growth and inhibition of growth is assessed by MTS assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Cohorts of EGFR TL/CCSP-rtTA and EGFR TD/CCSP-rtTA are put on doxycycline diet at 5 weeks of age to induce the expression of mutant EGFR. These mice undergo MRI after 6 to 8 weeks of doxycycline diet to document and quantify the lung cancer burden before being assigned to various treatment study cohorts. There is a minimum of 3 mice per treatment group. Mice are then treated either with vehicle (NMP 13 (10% 1-methyl-2-pyrrolidinone: 90% PEG-300) alone or WZ4002 at 25mg/kg gavage daily. After 2 weeks of treatment, these mice undergo a second round of MRI to document their response to the treatment. MRIs and tumor burden measurement are performed[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Discov. 2019 Jul;9(7):926-943.
- Eur J Med Chem. 2017 Oct 20;139:674-697.
- Oncotarget. 2020 Nov 3;11(44):3921-3932.
- Oncotarget. 2016 Oct 25;7(43):69760-69769.
- Oncotarget. 2015 Oct 13;6(31):31313-22.

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REFERENCES

[1]. Zhou W, et al. Novel mutant-selective EGFR kinase inhibitors against EGFR T790M.Nature. 2009 Dec 24;462(7276):1070-4.

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