Mobocertinib

Cat. No.: HY-135815

CAS No.: 1847461-43-1

Molecular Formula: $C_{32}H_{39}N_7O_4$

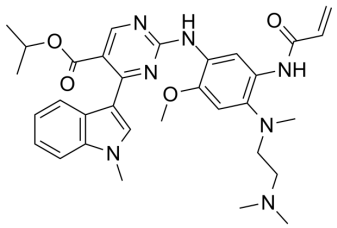
Molecular Weight: 585.7

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 : 25 mg/mL (42.68 mM; ultrasonic and warming and heat to 80°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7074 mL	8.5368 mL	17.0736 mL
	5 mM	0.3415 mL	1.7074 mL	3.4147 mL
	10 mM	0.1707 mL	0.8537 mL	1.7074 mL

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

In Vivo

1. Add each solvent one by one: 0.5% CMC/saline water
   Solubility: 25 mg/mL (42.68 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.27 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.13 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Mobocertinib (TAK-788) is an orally active and irreversible EGFR/HER2 inhibitor. Mobocertinib potently inhibits oncogenic variants containing activating EGFRex20ins mutations with selectivity over wild-type EGFR. Mobocertinib can be used in NSCLC research[1][2].

IC_{50} & Target	EGFR (WT)	EGFR exon 20 insertion	HER2

In Vitro

Mobocertinib (1.5 nM-10 μM; 7 days) inhibits LU0387 (NPH) cells with IC_{50} of 21 nM[1].

Mobocertinib (2 h) potently inhibits EGFR with common activating mutations (HCC827 (D), HCC4011 (L)) or with a T790M mutation (H1975 (LT)) more potently than WT EGFR (A431 (WT))[1].
Mobocertinib (0.1 nM-1 μM; 6 h) inhibits pEGFR and pERK1/2 in CUTO14 (ASV) cells[1].
Mobocertinib (0.3 nM-1 μM; 6 h) inhibits EGFR and downstream signaling[1].
Mobocertinib (0.01, 0.1 and 1 μM; 6 h) inhibits HER2 signaling in H1781 (HER2 Exon $20^{G776>VC}$), Ba/F3 (HER2 exon 20^{YVMA}) cells[2].

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

Cell Viability Assay[1]

Cell Line:	LU0387 (NPH) cells
Concentration:	1.5 nM-10 μM
Incubation Time:	7 days
Result:	Showed good inhibition activity for LU0387 (NPH) cells with IC_{50} of 21 nM.

Cell Viability Assay[1]

Cell Line:	A431 (WT), HCC827 (D), HCC4011 (L), H1975 (LT) cells
Concentration:	
Incubation Time:	2 h
Result:	Inhibited EGFR with common activating mutations of HCC827 (D), HCC4011 (L) cells and T790M mutation of H1975 (LT) with IC_{50}s of 4, 1.3 and 9.8 nM respectively, which more potently than WT EGFR (A431 (WT); IC_{50} of 35 nM).

Western Blot Analysis[1]

Cell Line:	CUTO14 (ASV) cells
Concentration:	0.1 nM-1 μM
Incubation Time:	6 h
Result:	Robustly inhibited EGFR signaling, reaching 80% and 100% inhibition of phosphorylated EGFR (pEGFR) at concentrations of 100 nM and 1 μM, respectively.

Western Blot Analysis[1]

Cell Line:	HCC827 (D), HCC4011 (L), H1975 (LT) cells
Concentration:	0.3 nM-1 μM
Incubation Time:	6 h
Result:	Potently inhibited EGFR and downstream signaling in HCC827 (D), HCC4011 (L) and H1975 (LT) cells.

Western Blot Analysis[2]

Cell Line:	H1781 (HER2 Exon $20^{G776>VC}$), Ba/F3 (HER2 exon 20^{YVMA}) cells
Concentration:	0.01, 0.1 and 1 μM
Incubation Time:	6 h

Result:	Inhibited HER2 signaling in H1781 and Ba/F3-HER2 exon 20^{YVMA} mutant cells at 0.1 μM with significantly decreased phosphorylations of HER2, AKT, and ERK1/2 in a dose-dependent manner.

In Vivo

Mobocertinib (3, 10, 30 mg/kg; p.o.; once daily for 20 days) significantly induces tumor growth inhibition[1].

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Animal Model:	Female Athymic Nude-$Foxn1^{nu}$ mice (human NSCLC H1975 LT tumor model)[1].
Dosage:	3, 10, 30 mg/kg
Administration:	Oral; once daily for 20 days.
Result:	Decreased the mean tumor volume by 44% and 92% when at 3 mg/kg and 10 mg/kg, respectively, relative to the tumor size of vehicle group. Induced a 76% tumor regression relative to the pretreatment tumor size at 30 mg/kg.

CUSTOMER VALIDATION

- Acta Pharm Sin B. 2023 Mar 10.
- Cells. 2021, 10(12), 3561.
- Lung Cancer. 2023 Jul, 181, 107250.
- Mol Pharm. 2022 Oct 21.
- JTO Clin Res Rep. 2023 Nov 27, 100614.

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REFERENCES

[1]. Gonzalvez F, et al. Mobocertinib (TAK-788): A Targeted Inhibitor of EGFR Exon 20 Insertion Mutants in Non-Small Cell Lung Cancer. Cancer Discov. 2021 Jul;11(7):1672-1687.

[2]. Han H, et al. Targeting HER2 Exon 20 Insertion-Mutant Lung Adenocarcinoma with a Novel Tyrosine Kinase Inhibitor Mobocertinib. Cancer Res. 2021 Oct 15;81(20):5311-5324.

Caution: Product has not been fully validated for medical applications. For research use only.

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