TAS0728

Cat. No.: HY-111553

CAS No.: 2088323-16-2

Molecular Formula: $C_{26}H_{32}N_8O_3$

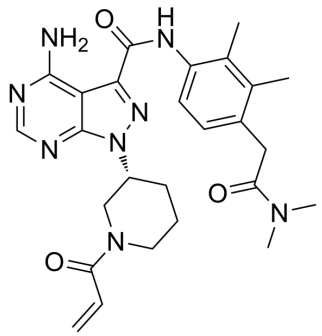
Molecular Weight: 504.58

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 : 125 mg/mL (247.73 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9818 mL	9.9092 mL	19.8185 mL
	5 mM	0.3964 mL	1.9818 mL	3.9637 mL
	10 mM	0.1982 mL	0.9909 mL	1.9818 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.12 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.12 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.12 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TAS0728 is a potent, selective, orally active, irreversible and covalent-binding HER2 inhibitor, with an IC_{50} of 13 nM. TAS0728 also shows IC_{50}s of 4.9, 8.5, 31, 65, 33, 25 and 86 nM for BMX、HER4、BLK、EGFR、JAK3、SLK and LOK respectively. Furthermore, TAS0728 exhibits robust and sustained inhibition of the phosphorylation of HER2HER3, and downstream effectors[1].

IC_{50} & Target				
	HER4	HER2	EGFR	BMX
	8.5 nM (IC_{50})	13 nM (IC_{50})	65 nM (IC_{50})	4.9 nM (IC_{50})

	BLK 31 nM (IC_{50})	JAK3 33 nM (IC_{50})	SLK 25 nM (IC_{50})	LOK 86 nM (IC_{50})

In Vitro

TAS0728 is a covalent-binding inhibitor of HER2 kinase and exhibits high selectivity for HER2 kinase. It also shows inhibitory activity against BMX, HER4, BLK, EGFR, JAK3, SLK, and LOK[1].

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

Cell Cytotoxicity Assay[1]

Cell Line:	HER2-amplified SK-BR-3/AU565/BT-474/NCI-N87/Calu-3 cells
Concentration:	
Incubation Time:	
Result:	The GI_{50} values of TAS0728 were 5.0/5.1/3.6/1.6/6.9 nM relatively for HER2-amplified SK-BR-3/AU565/BT-474/NCI-N87/Calu-3 cells. Inhibited the in vitro proliferation of five HER2-amplified cell lines. Showed potent inhibitory activities against cancer cell lines with HER2 amplification.

Western Blot Analysis[1]

Cell Line:	SK-BR-3 cells
Concentration:	30-300 nM
Incubation Time:	3 and 48 hours
Result:	Showed sustained inhibition of HER2, HER3, AKT and ERK phosphorylation.

In Vivo

TAS0728 reveals the sustained and targeted inhibition of phosphorylation of HER2, HER3, AKT and ERK. TAS0728 also shows the ability of tumor regression and low toxicity[1].

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

Animal Model:	Male nude mice
Dosage:	7.5, 15, 30 and 60 mg/kg
Administration:	Oral gavage; 7.5, 15, 30 and 60 mg/kg a day;14 days
Result:	Rapidly eliminated within 24 hours.

Animal Model:	Mice bearing NCI-N87 xenografts
Dosage:	60 mg/kg
Administration:	Oral gavage; 60 mg/kg a day; 14 days
Result:	Revealed sustained target inhibition of HER2, HER3, AKT and ERK.

Animal Model:	Mice with NCI-N87 HER2–amplified human gastric cancer
Dosage:	7.5, 15, 30 and 60 mg/kg
Administration:	Oral gavage; 7.5, 15, 30 and 60 mg/kg a day; 14 days

Result:	Well tolerated in all mice. Significant tumor regression was observed in mice treated with 60 mg/kg/day.

Animal Model:	NCI-N87 peritoneal dissemination model
Dosage:	30 and 60 mg/kg
Administration:	Oral gavage; 30and 60 mg/kg a day; 120 days
Result:	No evident toxicity, including diarrhea and body weight loss in the long-term dosing of TAS0728.

REFERENCES

[1]. Irie H, et al. TAS0728, A Covalent-binding, HER2-selective Kinase Inhibitor Shows Potent Antitumor Activity in Preclinical Models. Molecular cancer therapeutics. 2019;18(4):733-42. Epub 2019/02/23.

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