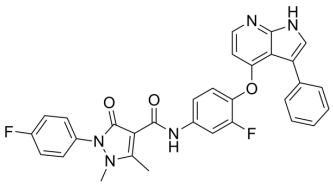
NPS-1034

Cat. No.:	HY-100509
CAS No.:	1221713-92-3
Molecular Formula:	$C_{31}H_{23}F_2N_5O_3$
Molecular Weight:	551.54
Target:	TAM Receptor; c-Met/HGFR; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis
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 : 34 mg/mL (61.65 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8131 mL	9.0655 mL	18.1311 mL
	5 mM	0.3626 mL	1.8131 mL	3.6262 mL
	10 mM	0.1813 mL	0.9066 mL	1.8131 mL

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

BIOLOGICAL ACTIVITY

Description

NPS-1034 is a dual inhibitor of AXL and MET with IC_{50}s of 10.3 and 48 nM, respectively.

IC_{50} & Target

IC50: 10.3 nM (AXL), 48 nM (MET)[1]

In Vitro

NPS-1034 is a dual inhibitor of AXL and MET with IC_{50}s of 10.3 and 48 nM, respectively.The expression and activity of AXL is significantly increased in HCC827/ER cells, and NPS-1034 treatment effectively inhibits its tyrosine phosphorylation[1]. NPS-1034 inhibits the viability of the MKN45 and SNU638 cell lines, which highly express the MET gene and p-MET (phosphorylated MET), with IC_{50} values of 112.7 and 190.3 nmol, respectively. In contrast, NPS-1034 inhibits AGS, KATOIII, NCI-N87, MKN1, MKN28, and MKN74 cell viability with IC_{50} values ranging from 1 μmol to more than 10 μmol. MET phosphorylation is dramatically decreased after treatment with NPS-1034 in the MKN45 cells, but not in the MKN28 cells. NPS-1034 inhibits hepatocyte growth factor (HGF)-stimulated MET autophosphorylation (Y1234/1235) in the AGS and MKN1 cell lines with IC_{50} values of <10 and <50 nmol, respectively. HGF-induced MET phosphorylation is completely inhibited by 50 nmol NPS-1034[2].

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

In Vivo	NPS-1034 inhibits tumor proliferation, which highly expresses p-MET. NPS-1034 treatment induces a clear decrease in the vascularization of the tumors. The expression of alpha-smooth muscle actin (α-SMA) is decreased in the tumor sections of mice treated with NPS-1034. NPS-1034-treated mice show virtually no weight loss, indicating that NPS-1034 is generally well tolerated[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	To perform the MTT assay, cells (0.5×10^4/well) are plated in 96-well sterile plastic plates and allowed to attach overnight. Cells are exposed to varying doses of NPS-1034 in medium containing 1% FBS. After 72 hours, 15 μL of MTT solution (5 mg/mL) is added to each well and plates are incubated for 4 hours. Crystalline formazan is solubilized with 100 μL of a 10% (w/v) SDS solution for 24 hours. Absorbance at 595 nm is read spectrophotometrically using a microplate reader[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Female severe combined immunodeficiency (SCID) mice (17 to 20 g, 6 weeks of age) are used. Tumors are grown by implanting 5×10^6 cells in Matrigel into the mouse flanks. Treatment of 5 mice per group is started when the tumors have reached a volume of 50 to 100 mm^3 with vehicle control or NPS-1034 (10 mg/kg, 5 days a week). NPS-1034 is administered orally. Treatment is stopped at the indicated day and mice are followed-up for tumor recurrence. To measure tumor size, the length (L) and width (W) of the tumor are measured with calipers, and tumor volume (TV) is calculated as $TV=(L\times W^2)/2$. Immunohistochemical staining is performed using a specific primary antibody, the EnVision Plus staining kit, and the APO-Direct terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling assay kit, according to the suppliers' instructions. Quantitative analysis of section staining is performed by counting immunopositive cells in 5 arbitrarily selected fields at ×40 magnification[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Medicina (Kaunas). 2022, 58(3), 355.

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REFERENCES

[1]. Rho JK, et al. MET and AXL inhibitor NPS-1034 exerts efficacy against lung cancer cells resistant to EGFR kinase inhibitors because of MET or AXL activation. Cancer Res. 2014 Jan 1;74(1):253-62.

[2]. Shin JS, et al. NPS-1034, a novel MET inhibitor, inhibits the activated MET receptor and its constitutively active mutants. Invest New Drugs. 2014 Jun;32(3):389-99.

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