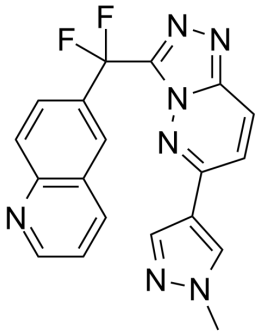
JNJ-38877605

Cat. No.:	HY-50683
CAS No.:	943540-75-8
Molecular Formula:	$C_{19}H_{13}F_2N_7$
Molecular Weight:	377.35
Target:	c-Met/HGFR
Pathway:	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 : ≥ 30 mg/mL (79.50 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6501 mL	13.2503 mL	26.5006 mL
5 mM	0.5300 mL	2.6501 mL	5.3001 mL
10 mM	0.2650 mL	1.3250 mL	2.6501 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 (5.51 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.51 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.51 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

JNJ-38877605 is an orally active ATP-competitive inhibitor of c-Met with an IC_{50} of 4 nM, 600-fold selective for c-Met than 200 other tyrosine and serine-threonine kinases[1][2]. JNJ-38877605 inhibits c-Met phosphorylation and regulates lipid accumulation. JNJ-38877605 can be used for tumor and metabolic disease reseach[3][4][5].

IC_{50} & Target

c-Met

4 nM (IC_{50})

In Vitro

JNJ-38877605 (0.5 μM, 24 h) inhibits CPNE1 (HY-P70097)-induced activation of the MET signaling pathway in A549 cells[4].
JNJ-38877605 (JNJ) (5, 10, 20 μM, 2, 5, 8 days) inhibits c-Met phosphorylation and results in less lipid accumulation and triglyceride (TG) content with no cytotoxicity in 3T3-L1 cells[5].

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

Western Blot Analysis[4]

Cell Line:	A549 cells
Concentration:	0.5 μM
Incubation Time:	24 h
Result:	Inhibited CPNE1 (HY-P70097)-induced MET phosphorylation and activation of the MET signaling pathway.

Western Blot Analysis[5]

Cell Line:	3T3-L1 cells
Concentration:	5,10,20 μM
Incubation Time:	2, 5, 8 day
Result:	Strongly inhibited c-Met phosphorylation without altering its total expression resulted in less lipid accumulation and triglyceride (TG) content with no cytotoxicity. Reduced the expression of adipogenic regulators, including CCAAT/enhancer-binding protein-α (C/EBP-α), peroxisome proliferator-activated receptor-γ (PPAR-γ), fatty acid synthase (FAS), acetyl CoA carboxylase (ACC), and perilipin A. Increased cAMP-activated protein kinase (AMPK) and liver kinase B-1 (LKB-1) phosphorylation but decreased ATP levels.

In Vivo

JNJ-38877605 (50 mg/kg, p.o., once daily for 13 days) counteractes radiation-induced invasiveness, promotes apoptosis in tumor xenografts[2].
JNJ-38877605 (40 mg/kg, p.o., once daily for 3 days) decreases in plasma concentration of IL8, GROa, uPAR Met-addicted GTL16 xenografts mice model[3].

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

Animal Model:	U251 human glioma cells and MDA-MB-231 human breast cancer cells transplanted tumor xenografts[2]
Dosage:	50 mg/kg
Administration:	Oral gavage (p.o.) once daily for 13 days
Result:	Counteracted radiation-induced invasiveness, promoted apoptosis.

Animal Model:	Met-addicted GTL16 xenografts mice model[3]
Dosage:	40 mg/kg
Administration:	Oral gavage (p.o.) once daily for 3 days
Result:	Decreased in the plasma levels of human IL-8 (from 0.150 to 0.050 ng/ml) and GROa (from 0.080 to 0.030 ng/ml).Diminished The blood concentration of uPAR also by more than 50% .Inhibited Met-addicted xenografts induced consistent changes in plasma concentration of

	IL8, GROa, uPAR and IL-6.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Stem Cell Res Ther. 2020 Jun 10;11(1):229.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Wang A, et.al. CPNE1 promotes non-small cell lung cancer progression by interacting with RACK1 via the MET signaling pathway. Cell Commun Signal. 2022 Jan 31;20(1):16.

[2]. Park YK, et.al. The Receptor Tyrosine Kinase c-Met Promotes Lipid Accumulation in 3T3-L1 Adipocytes. Int J Mol Sci. 2023 Apr 29;24(9):8086.

[3]. De Bacco F, et al. Induction of MET by ionizing radiation and its role in radioresistance and invasive growth of cancer. J Natl Cancer Inst. 2011 Apr, 103(8), 645-661.

[4]. Torti D, et al. A preclinical algorithm of soluble surrogate biomarkers that correlate with therapeutic inhibition of the MET oncogene in gastric tumors. Int J Cancer. 2012, 130(6), 1357-1366.

[5]. Perera T, et al. JNJ-38877605: a selective Met kinase inhibitor inducing regression of Met-driven tumor models. Presented at the 99th AACR Annual Meeting; 2008 Apr 12-16

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