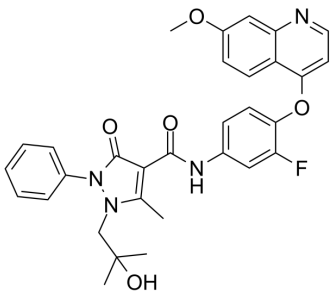
SYN1143

Cat. No.:	HY-18307
CAS No.:	913376-84-8
Molecular Formula:	$C_{31}H_{29}FN_4O_5$
Molecular Weight:	556.58
Target:	c-Met/HGFR
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (179.67 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7967 mL	8.9834 mL	17.9669 mL
	5 mM	0.3593 mL	1.7967 mL	3.5934 mL
	10 mM	0.1797 mL	0.8983 mL	1.7967 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: 2.5 mg/mL (4.49 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.49 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.49 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SYN1143 is a potent, selective and orally active dual inhibitor of c-Met/RON, with IC_{50}s of 4 and 9 nM, respectively. SYN1143 has weak inhibitory activity on Lck, Tie2, Src, and BTK with IC_{50}s ranging from 160 to 710 nM. SYN1143 can be used for the research of cancers that RON and c-Met are activated[1].

IC_{50} & Target

RON
9 nM (IC_{50})

In Vitro

SYN1143 (Compound I) (10-1000 nM; 1 h) inhibits c-Met-mediated signaling and functional activity in HT-29 and BxPC3 cells [1].

SYN1143 (10-1000 nM; 1 h) inhibits RON-mediated signaling and functional activity in NIH3T3 RON and BxPC3 cells[1].

SYN1143 (0.3-30 μM; 2 h or 3 d) inhibits c-Met signaling and cell proliferation in MC_3T_3-E_1 and $C_3H_{10}T_{1/2}$ cells[2].

SYN1143 (0.3-2 μM; 4-12 d) potentiates osteogenic differentiation of precursor cells[2].

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

Western Blot Analysis[1]

Cell Line:	HT-29 and BxPC3 cells
Concentration:	10, 30, 100, 300, 1000 nM
Incubation Time:	1 hours
Result:	Inhibited HGF-mediated c-Met phosphorylation and downstream signaling in a dose-dependent manner in both cell lines.

In Vivo

SYN1143 (10-100 mg/kg; p.o. for 22 d) inhibits the growth of c-Met-dependent and constitutively active RON-expressing tumors in mice[1].

SYN1143 (20-50 μg; transferred into calvarial defects) stimulates bone formation in critical-sized defects of mouse calvarial bone[2].

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

Animal Model:	Female CD1 nu/nu mice (6-8 weeks) bearing NIH3T3 TPR-Met s.c. tumors[1]
Dosage:	10, 30, 100 mg/kg
Administration:	Oral gavage either once or twice daily for 22 days
Result:	Significantly inhibited tumor growth at doses of 30 or 100 mg/kg once daily or at 30 mg/kg twice daily. Completely inhibited tumor growth at a dose of 100 mg/kg once daily. Did not adversely affect body weight.

REFERENCES

[1]. Zhang Y, et, al. Identification of a novel recepteur d'origine nantais/c-met small-molecule kinase inhibitor with antitumor activity in vivo. Cancer Res. 2008 Aug 15;68(16):6680-7.

[2]. Kim JW, et, al. Chemical inhibitors of c-Met receptor tyrosine kinase stimulate osteoblast differentiation and bone regeneration. Eur J Pharmacol. 2017 Jul 5;806:10-17.

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

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