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- Laborgeräte & Service

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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

SZABO-SCANDIC HandelsgmbH

Quellenstraße 110, A-1100 Wien

T. +43(0)1 489 3961-0

F. +43(0)1 489 3961-7

mail@szabo-scandic.com

www.szabo-scandic.com

linkedin.com/company/szaboscandic

PHA-665752

Cat. No.: HY-11107

CAS No.: 477575-56-7

Molecular Formula: $C_{32}H_{34}Cl_2N_4O_4S$

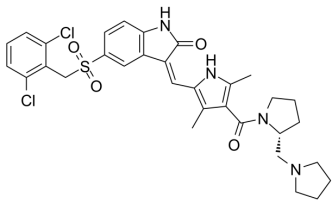
Molecular Weight: 641.61

Target: c-Met/HGFR; Autophagy; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Autophagy; 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 : 25 mg/mL (38.96 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5586 mL	7.7929 mL	15.5858 mL
	5 mM	0.3117 mL	1.5586 mL	3.1172 mL
	10 mM	0.1559 mL	0.7793 mL	1.5586 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 (3.90 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.90 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PHA-665752 is a selective, ATP-competitive, and active-site inhibitor of the catalytic activity of c-Met kinase (K_i=4 nM; IC_{50}=9 nM). PHA-665752 exhibits >50-fold selectivity for c-Met compared with a panel of diverse tyrosine and serine-threonine kinases. PHA-665752 induces apoptosis and cell cycle arrest, and exhibits cytoreductive antitumor activity[1][2].

IC_{50} & Target

Ki: 4 nM[1]

IC50: 9 nM (c-Met)[1]

In Vitro

PHA-665752 is a potent and ATP-competitive inhibitor of c-Met kinase activity with a K_i of 4 nM and an IC_{50} of 9 nM[1].
PHA-665752 exhibits >50-fold selectivity for c-Met enzyme compared with the majority of kinases evaluated[1].
PHA-665752 shows potent inhibition of c-Met RTK autophosphorylation in NIH3T3 cells engineered to express high levels of c-Met and hepatocyte growth factor (HGF)[1].
PHA-665752 inhibits HGF-stimulated or constitutive phosphorylation of mediators of downstream of c-Met such as Gab-1, ERK, Akt, STAT3, PLC-γ, and FAK in multiple tumor cell lines[1].
PHA-665752 (0-1.25 μM; 18 hours) potently inhibits HGF and c-Met-driven phenotypes such as cell growth (proliferation and survival), cell motility, invasion, and/or morphology of a variety of tumor cells[1].
PHA-665752 (0-1.25 μM; 72 hours) induces apoptosis in both the presence and absence of HGF at concentrations that inhibited tyrosine phosphorylation of c-Met in GTL-16 cells[1].
PHA-665752 (0.0125-0.2 μM; 4 hours) potent inhibits HGF-induced c-Met phosphorylation in A549 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	S114 cells, GTL-16 cells, NCI-H441 cells, or BxPC-3 cells
Concentration:	0 μM, 0.002 μM, 0.01 μM, 0.05 μM, 0.25 μM, 1.25 μM
Incubation Time:	18 hours
Result:	Potently inhibited HGF and c-Met-driven cell growth.

Apoptosis Analysis[1]

Cell Line:	GTL-16 cells
Concentration:	0 μM, 0.002 μM, 0.01 μM, 0.05 μM, 0.25 μM, 1.25 μM
Incubation Time:	72 hours
Result:	Induced apoptosis in both the presence and absence of HGF at concentrations that inhibited tyrosine phosphorylation of c-Met in GTL-16 cells. Immunoblot Analysis.

Western Blot Analysis[1]

Cell Line:	A549 cells
Concentration:	0.0125 μM, 0.025 μM,0.05 μM,0.1 μM,0.2 μM
Incubation Time:	4 hours
Result:	Potent inhibited HGF-induced c-Met phosphorylation in A549 cells.

In Vivo

PHA-665752 (7.5-30 mg/kg/day; i.v. ; for 9 days) exhibits statistically significant dose-dependent tumor growth inhibition of 68%, 39%, and 20% of vehicle control at the 30 mg/kg/day, 15 mg/kg/day, and 7.5 mg/kg/day doses, respectively[1].
PHA-665752 shows a potent cytoreductive activity in a gastric carcinoma xenograft model[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female athymic mice (nu/nu, 8–12 weeks) bearing S114 or GTL-16 tumor xenografts[1]
Dosage:	7.5 mg/kg/day, 15 mg/kg/day, 30 mg/kg/day
Administration:	Intravenous injection; for 9 days
Result:	Demonstrated statistically significant dose-dependent tumor growth inhibition.

CUSTOMER VALIDATION

- Cancer Lett. 2020 Dec 28;495:41-52.
- Cell Death Dis. 2022 Apr 21;13(4):387.
- Int J Cancer. 2019 Aug 1;145(3):748-762.
- Respir Res. 2020 Aug 14;21(1):215.
- Mol Cancer Ther. 2018 Mar;17(3):603-613.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Christensen JG, et al. A selective small molecule inhibitor of c-Met kinase inhibits c-Met-dependent phenotypes in vitro and exhibits cytoreductive antitumor activity in vivo. Cancer Res. 2003 Nov 1;63(21):7345-55.

[2]. Ma PC. et al. A selective small molecule c-MET Inhibitor, PHA665752, cooperates with rapamycin. Clin Cancer Res. 2005 Mar 15;11(6):2312-9.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA