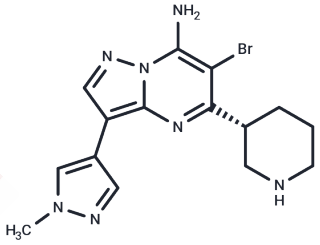
Data Sheet (Cat.No.T2517)

TargetMol

SCH900776

Chemical Properties



CAS No. : 891494-63-6

Formula: C15H18BrN7

Molecular Weight: 376.25

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	SCH900776 (MK-8776) is an agent targeting cell cycle checkpoint kinase 1 (Chk1) with potential radiosensitization and chemosensitization activities.
Targets(IC50)	CDK,Chk
In vitro	Administering 4 mg/kg of SCH 900776 30 minutes after gemcitabine triggers the γ-H2AX biomarker, while a dose of 8 mg/kg of SCH 900776 boosts tumor pharmacodynamics and degradation response. Incremental increases to 16 mg/kg and 32 mg/kg of SCH 900776 further improve tumor response. Notably, within BALB/c mice, the dose of SCH 900776 correlates with strong biomarker activation, independent of gemcitabine's intensified hematologic toxicity.
In vivo	After 24 hours of exposure to hydroxyurea, SCH 900776 induces a dose-dependent loss of DNA replication capacity. SCH 900776 enhances the response of γ-H2AX to hydroxyurea, 5-fluorouracil, and cytarabine. By combining with antimetabolites, SCH 900776 triggers the accumulation of γ-H2AX within 2 hours, indicating replication fork collapse and subsequent double-strand DNA breaks. Additionally, SCH 900776 inhibits the accumulation of Chk1 pS296 autophosphorylation in a dose-dependent manner. SCH 900776 is a weak inhibitor of Chk2 and CDK2, with IC50 values of 1.5 μM and 0.16 μM, respectively. SCH 900776 does not significantly inhibit human liver microsomal cytochrome P450 subtypes 1A2, 2C9, 2C19, 2D6, and 3A4.
Kinase Assay	The Millipore Kinase Profiler service is used to generate general selectivity data for SCH 900776 against a broad range of serine/threonine and tyrosine kinases. Assays are typically run at two concentrations of SCH 900776 (0.5 and 5 μM), at a fixed (10 μM) concentration of ATP. Data are provided as percent activity remaining, relative to uninhibited controls.
Cell Research	For cell growth assays, cells are seeded at low density (500-1000 cells) in 96-well plates and then incubated with drug for 24 h (8 wells per concentration). Following treatment, cells are washed and grown in fresh media for 5-7 days at 37°C. Prior to attaining confluence, cells are washed, lysed, and stained with Hoechst 33258. Fluorescence is read on a microplate spectrofluorometer. Results are expressed as mean and standard error for the concentration of drug that inhibited growth by 50%.

Solubility Information

Solubility	DMSO: 150 mg/mL (398.67 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4 mg/mL (10.63 mM),Sonication is recommended. 10% DMSO+90% Saline: 10 mg/mL (26.58 mM),Suspension. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.6578 mL	13.289 mL	26.5781 mL
5 mM	0.5316 mL	2.6578 mL	5.3156 mL
10 mM	0.2658 mL	1.3289 mL	2.6578 mL
50 mM	0.0532 mL	0.2658 mL	0.5316 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Guzi TJ, et al. Mol Cancer Ther, 2011, 10(4), 591-602.
Ou J, Li H, Qiu P, et al. CDK9 modulates circadian clock by attenuating REV-ERBα activity. Biochemical and Biophysical Research Communications. 2019 Jun 11;513(4):967-973
Montano R, et al. Mol Cancer Ther, 2012, 11(2), 427-438.
Schenk EL, et al. Clin Cancer Res, 2012, 18(19), 5364-5373.
Ou J, Li H, Qiu P, et al. CDK9 modulates circadian clock by attenuating REV-ERBα activity[J]. Biochemical and biophysical research communications. 2019 Jun 11;513(4):967-973.