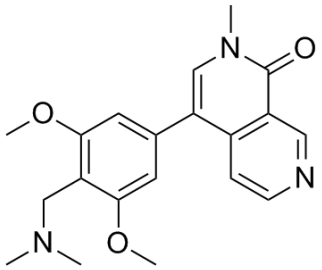
BI-7273

Cat. No.:	HY-100351
CAS No.:	1883429-21-7
Molecular Formula:	$C_{20}H_{23}N_3O_3$
Molecular Weight:	353.41
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
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 : 10 mg/mL (28.30 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8296 mL	14.1479 mL	28.2957 mL
	5 mM	0.5659 mL	2.8296 mL	5.6591 mL
	10 mM	0.2830 mL	1.4148 mL	2.8296 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: ≥ 1 mg/mL (2.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 1 mg/mL (2.83 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1 mg/mL (2.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BI-7273 is a selective, and cell-permeable BRD9 inhibitor, with an IC_{50} and a K_d of 19 and 0.75 nM; also shows high effect on BRD7, with an IC_{50} and a K_d of 117 nM and 0.3 nM.

IC_{50} & Target

IC50: 19 nM (BRD9), 117 nM (BRD7)[1]
Kd: 0.75 nM (BRD9), 0.3 nM (BRD7)[1]

In Vitro

BI-7273 is a selective, and cell-permeable BRD9 inhibitor, with an IC_{50} and a K_d of 19 and 0.75 nM; also shows high effect on

BRD7, with an IC_{50} and a K_d of 117 nM and 0.3 nM. BI-7273 also has slight activity against a panel of kinases such as CECR2, BRPF1, BRD1, CREBBP, EP300, FALZ, TAF1(2) and TAF1L(2), with K_ds of 8.8 nM, 210 nM, 2600 nM, 8600 nM, 10000 nM, 850 nM, 1000 nM, and 1200 nM, respectively. BI-7273 (1 μM) is active in U2OS cell lines. BI-7273 blocks EOL-1 cell proliferation with EC_{50} of 1400 nM[1].

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

PROTOCOL

Kinase Assay [1]

His-tagged BRD9 is immobilized to a density of 2000-4000 RUs on flow cells 3 and 4 of a Biacore NTA-chip. Carbonic anhydrase II is immobilized at a similar density on flow cell 2 and a blank reference surface is generated on flow cell 1. The buffer is then switched to assay buffer (HBS-P+ = 10 mM HEPES, pH 7.4, 150 mM NaCl, 0.05 % P20 + 5 % DMSO) and the chip equilibrated for several hours before use for K_d determinations. To be able to correct for differences in bulk solvent refractive index caused by small variations in the DMSO concentration solvent correction samples are included at the beginning and end of the run. Compounds (BI-7273, etc.) are injected in concentration series (1:1 dilutions, 7 different concentrations), starting with a maximum concentration that is approximately 10-20-fold higher than the expected K_d. The concentration series are prepared in 96-well plates. In the case that the dilution window chosen for a particular compound does not appropriately bracket the K_d of the compound the measurement is repeated with an optimized starting concentration. Positive and negative control samples are included at regular intervals to be able to monitor the performance of the assay. CBS is used as a positive control for carbonic anhydrase II to check for integrity of the reference protein at regular intervals. To correct for the excluded volume effect a DMSO calibration series is prepared and the calibration samples are measured at the beginning and end of each run. K_d values are determined and averaged[1].

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

Cell Assay [1]

Cells are grown in 50 μL medium for 7 days starting with 500 and with 1000 cells per well of a 384 well plate in the presence of varying concentrations of compound (BI-7273, etc.) before measuring viability via cellular ATP levels using the cell titer glow assay[1].

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

REFERENCES

[1]. Martin LJ, et al. Structure-Based Design of an in Vivo Active Selective BRD9 Inhibitor. J Med Chem. 2016 May 26;59(10):4462-75.

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