BI-9564

Cat. No.: HY-100352

CAS No.: 1883429-22-8

Molecular Formula: $C_{20}H_{23}N_3O_3$

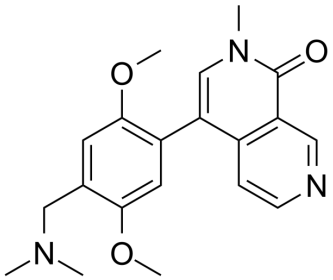
Molecular Weight: 353.41

Target: Epigenetic Reader Domain

Pathway: Epigenetics

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 8.33 mg/mL (23.57 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: ≥ 0.83 mg/mL (2.35 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.83 mg/mL (2.35 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.83 mg/mL (2.35 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BI-9564 is a potent, selective and cell-permeable BRD9/BRD7 bromodomains inhibitor, with IC_{50}s of 75 nM and 3.4 μM and K_d s of 14 nM and 239 nM, respectively. BI-9564 has an IC_{50} of > 100 μM for BET family[1].

IC_{50} & Target

BRD9	BRD9	BRD7	BRD7
75 nM (IC_{50})	14 nM (Kd)	3.4 μM (IC_{50})	239 nM (Kd)

In Vitro

BI-9564 (<5 μM) shows no activity against 324 kinases, and at 10 μM, an inhibition >40% is observed for only 2 out of 55

	GPCRs. BI-9564 has antiproliferative effect on human acute myeloid eosinophilic leukemia cell line EOL-1, with EC_{50} of 800 nM[1]. BI-9564 shows K_d of 73 nM for BRD7, and is >10-fold more selective for BRD9 over the highly homologues bromodomain BRD7, which has been implied as a tumor suppressor and is down-regulated in cancer cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	BI-9564 (180 mg/kg, p.o.) shows attractive ADME/PK profiles for in vivo proof-of-concept studies. BI-9564 results in a modest but significant additional survival benefit of 2 days compared to survival of the control group in a xenograft model of human AML[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cells are grown in 50 µL medium as specified by the supplier 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 before measuring viability via cellular ATP levels using the cell titer glow assay. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Female CIEA-NOG mice are engrafted intravenously with 1×10^7 EOL-1 AML cells stably expressing luciferase and GFP. Following injection of the cells animals are randomized based on body weight (n=10/group). Treatment starts on day 5 with either 0.5% Natrosol or BI-9564 formulated with 0.5% Natrosol. All doses are calculated relative to the mouse body weight on the treatment day. BI-9564 and the vehicle control are administered orally with a dosing volume of 10 mL/kg body weight. BI-9564 is administered daily from day 5 until 17 and from day 20 until 22. Dosing is interrupted on day 18 for two days as one mouse in the treatment group reaches -15% body weight loss. Tumour load is measured 2-3 times weekly based on bioluminescence imaging. The following scoring system is used: score 0, no clinical signs; score 1, tail or hind limb weakness. Animals are sacrificed based on severity criteria including appearance of paralysis score 1 and/or body weight loss exceeding -18%. In S54 this tumor mouse model body weight changes can occur due to increased tumor load or due to intolerability. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- bioRxiv. 2023 Apr 3.

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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.

[2]. Rezaul M. Karim, et al. An Advanced Tool To Interrogate BRD9. J. Med. Chem., 2016, 59 (10), pp 4459-4461

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