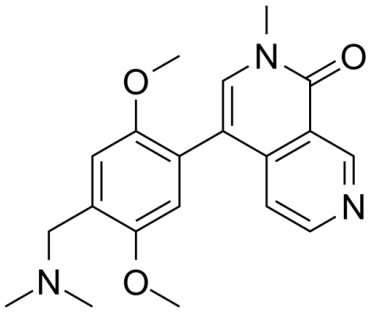
Data Sheet

Product Name:	BI-9564
Cat. No.:	CS-5888
CAS No.:	1883429-22-8
Molecular Formula:	C20H23N3O3
Molecular Weight:	353.41
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
Solubility:	DMSO : 8.33 mg/mL (23.57 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

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]. IC50 & Target: Kd: 20 nM (BRD9) **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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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. **Animal Administration:** BI-9564 is formulated with 0.5% Natrosol.[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.

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

CAIndexNames:

4-(4-((dimethylamino)methyl)-2,5-dimethoxyphenyl)-2-methyl-2,7-naphthyridin-1(2H)-one

SMILES:

CN(C)CC1=CC(OC)=C(C(C2=C3C=NC=C2)=CN(C)C3=O)C=C1OC

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

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