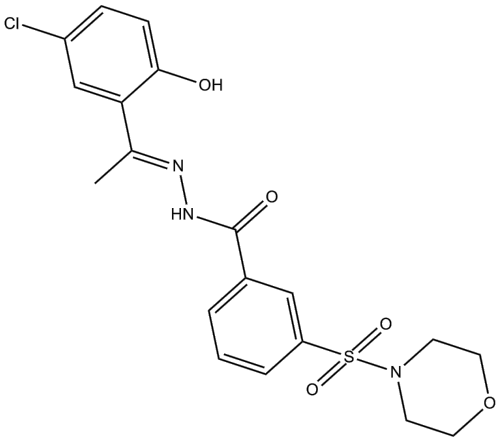
Product Data Sheet

Product Name: SP2509
Cat. No.: GC14631

Chemical Properties

Cas. No.	1423715-09-6		
Chemical Name	(E)-N'-(1-(5-chloro-2-hydroxyphenyl)ethylidene)-3-(morpholinosulfonyl)benzohydrazide		
SMILES	OC1=CC=C(Cl)C=C1/C(C)=N/NC(C2=CC=CC(S(=O)(N3CCOCC3)=O)=C2)=O		
Formula	$C_{19}H_{20}ClN_3O_5S$	M.Wt	437.9
Solubility	≥ 19.45mg/mL in DMSO	Storage	4°C, protect from light
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			

Protocol

Kinase experiment [1]:

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SP2509 activity assay	Test compounds were diluted to 20 × the desired test concentration in 100% dimethyl sulfoxide and 2.5 μl of the diluted drug sample was added to a black 384-well plate. The LSD1 enzyme stock was diluted 17-fold with assay buffer and 40 μl of the diluted LSD1 enzyme was added to the appropriate wells. Substrate, consisting of horseradish peroxidase, dimethyl K4 peptide corresponding to the first 21 amino acids of the N-terminal tail of histone H3, and 10-acetyl-3,7-dihydroxyphenoxazine was then added to wells. Resorufin was analyzed on a plate reader with an excitation wavelength of 530 nm and an emission wavelength of 595 nm.

Cell experiment [1]:

Cell lines	OCI-AML3 and MOLM13
Preparation method	Limited solubility. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reaction Conditions	16 h
Applications	SP2509 inhibits LSD1 activity, reduces colony growth and induces apoptosis of cultured AML cells. SP2509 treatment also inhibits the association of LSD1 with CoREST, increases promoter-specific H3K4Me3 and induces p53, p21 and C/EBPα in AML cells. Furthermore, treatment with SP2509 induces differentiation of cultured and primary AML cells

Animal experiment [1]:

Animal models	NOD/SCID mice

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Dosage form	25 mg/kg SP2509 administered twice per week (Tuesday and Thursday) intraperitoneally for 3 weeks
Applications	Treatment with either SP2509 improves the median survival of the mice infused with OCI-AML3 cells (37 and 36.5 days, respectively, versus 19.5 days for vehicle control). Notably, combined treatment with panobinostat and SP2509 further improves the median survival of the mice (44.5 days), as compared with treatment with SP2509 or panobinostat alone (P<0.01).
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

1. Fiskus W, Sharma S, Shah B et al. Highly effective combination of LSD1 (KDM1A) antagonist andpan-histone deacetylase inhibitor against human AML cells. Leukemia. 2014 Nov;28(11):2155-64

Background

SP2509 is a novel Lysine specific demethylase 1 (LSD1) antagonist (IC50 = 13nM) with no effect on MAO-A and MAO-B. [1]
LSD1 demethylates mono-/di-methylated lysine 4 on histone H3. High expression of LSD1 is associated with poor prognosis in cancer. [2]
In cultured human AML cells, SP2590 inhibited LSD1 activity, deplete colony growth and elicit apoptosis. SP2590 also inhibited the LSD1 binding to CoREST, increase promoter-specific H3K4Me3 and induces p53, p21 and C/EBPα in AML cells. Moreover, SP2590 promotes differentiated of cultured and primary AML cell. [1]
In mice carrying AML xenografts, SP2590 treatment alone significantly improved the survival of mice and co-treatment with an-HDAC inhibitor (HDI) panobinostat (PS) exhibited superior in vivo activity. [1]

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References:

1. Fiskus W, Sharma S, Shah B, Portier BP, Devaraj SG, Liu K, Iyer SP, Bearss D, Bhalla KN. Highly effective combination of LSD1 (KDM1A) antagonist andpan-histone deacetylase inhibitor against human AML cells. Leukemia. 2014 Nov;28(11):2155-64.

2. Zhao ZK, Yu HF, Wang DR, Dong P, Chen L, Wu WG, Ding WJ, Liu YB. Overexpression of lysine specific demethylase 1 predicts worse prognosis in primary hepatocellular carcinoma patients. World J Gastroenterol. 2012 Dec 7;18(45):6651-6.

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

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