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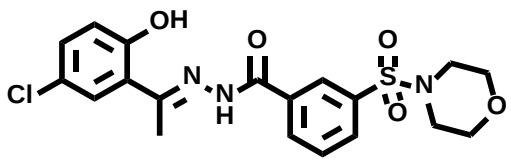
Reversible LSD1 Inhibitor – HCI-2509 (SP2509, LSD1-C12)

Chemical Name: (E)-N'-(1-(5-chloro-2-hydroxyphenyl)ethylidene)-3-(morpholinosulfonyl)benzohydrazide



Molecular Weight:	437.90
Formula:	$C_{19}H_{20}ClN_3O_5S$
Purity:	≥98%
CAS#:	1423715-09-6
Solubility:	DMSO up to 50 mM
Storage	Powder: 4 ºC 1 year DMSO: 4 ºC 3 months -20 ºC 1 year

Biological Activity:

HCI-2509 (also named as SP2509 or LSD1-C12) is a highly potent, specific, and reversible Lysine Specific Demethylase-1 (LSD1) inhibitor. It inhibits LSD1 in biochemical assay with an IC_{50} ~13 nM, and has no activity against monoamine oxidase proteins MAO-A and MAO-B (>300 µM). HCI-2509 is a non-competitive inhibitor to bind LSD1, changes its solution dynamics in a manner distinct from TCP. It has minimal inhibition of CYPs and hERG, shows cellular activity against several cancer cell lines including endometrial, breast, colorectal, pancreatic, and prostate cancer (IC_{50} ~0.3-2.5 µM). HCI-2509 displayed sing-agent efficacy in multiple xenograft models and had good PK/PD relationship by using tumor histone H3K4 and H3K9 methylation. HCI-2509 serves as a very useful chemical probe to study the target biology of LSD1.

How to Use:

In vitro: HCI-2509 was used at 1 µM in vitro.

In vivo: HCI-2509 was administered through IP injection at 25-30 mg/kg once per day in xenografts models.

Reference:

1. Fiskus W, et al. Highly effective combination of LSD1 (KDM1A) antagonist and pan-histone deacetylase inhibitor against human AML cells. (2014) Leukemia. 28(11):2155-64.
2. Sorna V, et al. High-Throughput Virtual Screening Identifies Novel N'-(1-Phenylethylidene)-benzohydrazides as Potent, Specific, and Reversible LSD1 Inhibitors. (2013) J Med Chem. 56(23):9496-508.
3. Wiles ET, et al. BCL11B is up-regulated by EWS/FLI and contributes to the transformed phenotype in Ewing sarcoma. (2013) PLoS One. 8(3):e59369.
4. Bret J. Stephens, et al.: Activity of the LSD1 inhibitor HCI-2509 in ER-negative breast cancer cells. (2012) AACR Chicago. Abstract 1045. Cancer Research: April 15, 2012; Volume 72, Issue 8, Supplement 1.
5. Emily R, et al. Inhibition of LSD1 disrupts global EWS/ETS transcriptional function in Ewing sarcoma. (2014) AACR San Diego. Abstract 3679.