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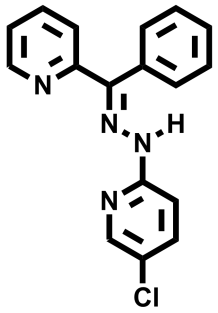
Jumonji Histone Demethylase Inhibitor – JIB-04 (NSC693627)

Chemical Name: (E)-5-chloro-2-(2-(phenyl(pyridin-2-yl)methylene)hydrazinyl)pyridine



Molecular Weight:	308.76
Formula:	$C_{17}H_{13}ClN_4$
Purity:	≥98%
CAS#:	199596-05-9
Solubility:	DMSO up to 50 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

JIB-04 (NSC693627, E-isomer) is a potent, selective and cell permeable Jumonji histone demethylase inhibitor. Unlike the other known inhibitors, JIB-04 is not a competitive inhibitor of a-ketoglutarate. It inhibits the demethylase activity of Jumonji enzymes in vitro, with IC_{50} ~230 nM for JARID1A (KDM5A), ~440 nM for JMJD2A (KDM4A) and JMJD2B (KDM4B), ~340 nM for JMJD2E (KDM2E), and ~1 μM for JMJD3 (KDM6B) and JMJD2C (KDM4C). JIB-04 blocks Jumonji demethylase activity in cells and consequently inhibits cell growth, without affecting other a-ketoglutarate-dependent hydroxylases or histone-modifying enzymes, especially HDACs. JIB-04 alters transcriptional programs in cancer but not in normal cells, leading to cancer-specific cell death. Importantly, in vivo, JIB-04 lowers histone demethylase activity in tumors, reduces tumor burden and prolongs survival of mice in an aggressive breast cancer model.

How to Use:

In vitro: JIB-04 was used at 1 μM final concentration in various in vitro assays.

In vivo: JIB-04 was administered 2–3 times weekly by IP injection at 110 mg/kg in sesame oil (H358 xenografts) or by gavage in Cremophor EL at 55 mg/kg (A549 xenografts) for 4-6 weeks.

Reference:

1. Wang L, et al. A small molecule modulates Jumonji histone demethylase activity and selectively inhibits cancer growth. (2013) Nat Commun. 4:2035