For Research Use Only

MI-503

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Catalog Number: CM04574

产品信息

Catalog Number:
CM04574

CAS号:
1857417-13-0

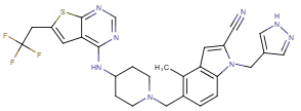
分子式:
$C_{28}H_{27}F_3N_8S$

主要靶点:
Histone Methyltransferase|Epigenetic Reader Domain

主要通路:
表观遗传

分子量:
564.63

溶解度:
H2O:Insoluble,DMSO:45 mg/mL (79.7 mM),Sonification is recommended.



靶点活性

Menin-MLL:4.7 nM (cell free)

体外活性

Treatment of murine bone marrow cells (BMC) transformed with the mLL-AF9 oncogene with MI-503 results in substantial growth inhibition (GI50: 0.22 μM). The cell growth inhibitory effect of MI-503 is time-dependent, with a pronounced effect achieved after 7-10 days of treatment.

体内活性

MI-503 achieves high level in peripheral blood following a single intravenous or oral dose, while also showing high oral bioavailability (75%). MI-503 induces strong inhibition of tumor growth with once-daily intraperitoneal (i.p.) administration. Treatment with MI-503 results in an over 80% reduction in MV4;11 tumor volume and complete tumor regression in two mice. Ten consecutive days of treatment with MI-503 results in a marked delay in progression of mLL leukemia in mice and significantly reduces leukemia tumor burden. Treatment with MI-503 and MI-463 leads to markedly reduced expression of Hoxa9 and Meis1.

动物实验

For efficacy studies in MV4;11 subcutaneous xenograft mice model, 5×10^6 cells are injected into the 4-6 week old female BALB/c nude mice. Treatment is started when the tumor size reached ~100 mm^3. Vehicle (25% DMSO, 25% PEG400, 50% PBS) or compounds (MI-463 or MI-503) are administrated once daily at designated doses using i.p. injections.

细胞实验

Leukemia cells are treated with MI-503 or 0.25% DMSO and cultured at 37 °C for 7 days. Media is changed on day 4, viable cell numbers are restored to the original concentration and MI-503 are re-supplied. MTT cell proliferation assay kit is then employed, and plates are read for absorbance at 570 nm using a microplate reader.

描述

MI-503 is a highly effective and orally bioavailable inhibitor of the menin-mLL interaction.

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years