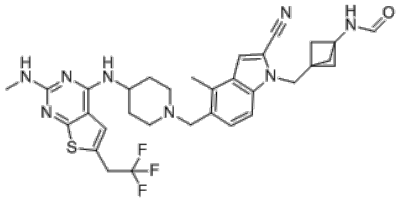
ProbeChem®
Expedite Your Scientific Research

WWW.PROBECHEM.COM

Data Sheet

Global Supplier of Chemical Probes, Inhibitors & Agonists.

Product Name	:	MI-3454
Cat. No.	:	PC-72046
CAS No.	:	2134169-43-8
Molecular Formula	:	$C_{32}H_{35}F_3N_8OS$
Molecular Weight	:	636.742
Target	:	Histone Methyltransferase (HMTase)
Solubility	:	10 mM in DMSO



Biological Activity

MI-3454 (MI 3454) is a highly potent, orally bioavailable inhibitor of the **menin-MLL1** interaction with IC50 of 0.51 nM, 60-fold improvement over MI-503.
MI-3454 inhibits growth of human MLL leukemic cell lines (MLL-tr): MV-4-11, MOLM-13, KOPN-8, SEM, RS4-11 with GI50 values of 7-27 nM in MTT cell viability assays, does not significantly (>100-fold) affect the growth of leukemic cells without MLL1 translocations.
MI-3454 (50 nM or lower) led to downregulated expression of HOXA9 and MEIS1 in MV-4-11 and MOLM13 cells, also reduced other MLL fusion target genes, including MEF2C, DLX2, HOXA10, PBX3, and FLT3.
MI-3454 demonstrated strong reduction of cell proliferation and downregulation of HOXA9 and MEIS1 expression in mouse bone marrow cells transformed with the MLL-AF9 oncogene but not in bone marrow cells transformed with HOXA9 and MEIS1 oncogenes.
MI-3454 induces leukemia regression in xenograft model of MLL leukemia through on-target activity.
MI-3454 (3–12 nM) substantially reduced clonogenic potential in MLL leukemia patient samples with MLL1 translocations or NPM1 mutations, MI-3454 induced complete remission or blocks leukemia progression in PDX models of MLL leukemia.

References

Klossowski S, et al. ***J Clin Invest***. 2020 Feb 3;130(2):981-997.

Miao H, et al. ***Blood***. 2020 Dec 17;136(25):2958-2963.

E-mail: tech@probechem.com