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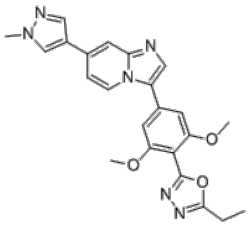
Data Sheet

Global Supplier of Chemical Probes, Inhibitors & Agonists.

Product Name	:	SK-124
Cat. No.	:	PC-49563
CAS No.	:	2760404-50-8
Molecular Formula	:	$C_{23}H_{22}N_6O_3$
Molecular Weight	:	430.468
Target	:	Salt Inducible Kinase (SIK)
Solubility	:	10 mM in DMSO



Biological Activity

SK-124 (SK124) is a potent, selective, orally active **SIK2/SIK3** inhibitor with IC50 of 8.8/11.3 nM in cell-based NanoBRET assays, 15-fold selectivity versus SIK1.
SK-124 potently inhibits SIK2/SIK3 with IC50 of 0.41/1.2 nM in radioisotope kinase assays, respectively.
SK-124 displays acceptable oral bioavailability in mice, robust stability in human, rat, and mouse liver microsomes, no inhibition of cytochrome P450 enzymes.
SK-124 exhibits no significant off-target activities at 10 μM in the Eurofins SafetyScreen44 panel, PDGFRα (IC50=15.8 nM) is the major off-target kinase.
SK-124 engages endogenous SIK2 in murine osteocyte-like Ocy454 cells, reduces phosphorylation of SIK substrates HDAC4/HDAC5 and CRTC2 in murine Ocy454 and human Saos2 cells, promotes CRTC2 (EC50=128 nM in) and HDAC5 nuclear translocation, and regulated SIK target gene [SOST and TNFSF11 (also known as RANKL)] expression in a PTH-like manner without causing cytotoxicity.
Oral SK-124 (40 mg/kg) treatment increased P1NP and C terminal telopeptide (CTX) compared with oral vehicle solution in a manner similar to that of once-daily subcutaneous PTH treatmentparathyroid hormone (PTH).
3 wk of 40 mg/kg SK-124 treatment led to changes consistent with intermittent PTH therapy and inducible SIK2/SIK3 deletion including increased trabecular bone in the primary spongiosa (PS), modest growth plate expansion, and increased TRAP-positive osteoclasts in the proximal tibia.

References

Sato T, et al. ***Proc Natl Acad Sci U S A.*** 2022 Dec 13;119(50):e2214396119.

Caution: Product has not been fully validated for medical applications. Lab Use Only!

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