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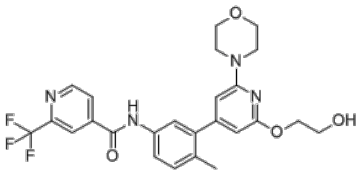
Data Sheet

Global Supplier of Chemical Probes, Inhibitors & Agonists.

Product Name	:	LXH254
Cat. No.	:	PC-35635
CAS No.	:	1800398-38-2
Molecular Formula	:	$C_{25}H_{25}F_3N_4O_4$
Molecular Weight	:	502.494
Target	:	Raf
Solubility	:	10 mM in DMSO



Biological Activity

LXH254 (Naporafenib, LXH 254) is a highly potent, selective B/C **RAF** inhibitor with Kd of 1.3/3.6 nM respectively, shows less activity against ARAF.
LXH254 (Naporafenib) inhibits pMEK and cell proliferation in Calu-6 cells with EC50 of 0.014 uM and 0.47 uM, respectively
LXH254 (Naporafenib) showed a high level of selectivity on a panel of 456 kinases, demonstrating greater than 98% on-target binding to BRAF, BRAFV600E, and CRAF at 1 uM and very few off-targets, with DDR1 (>99%), DDR2 (84%), and PDGFRb (>99%) the only kinases with binding >80% at 1 uM.
LXH254 (Naporafenib) was active in models harboring BRAF alterations, including atypical BRAF alterations coexpressed with mutant K/NRAS, and NRAS mutants, but had only modest activity in KRAS mutants. LXH254 caused paradoxical activation of MAPK signaling in a manner similar to dabrafenib in cells expressing only ARAF.
LXH254 (Naporafenib) demonstrated tumor regression in the Calu-6 xenograft nude rat model.

References

Monaco KA, et al. ***Clin Cancer Res.*** 2021 Apr 1;27(7):2061-2073.
2. Ramurthy S, et al. ***J Med Chem.*** 2020 Mar 12;63(5):2013-2027.
3. Negrao MV, et al. ***J Thorac Oncol.*** 2020 Oct;15(10):1611-1623.

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