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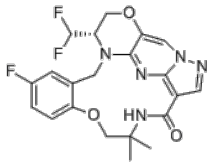
Data Sheet

Global Supplier of Chemical Probes, Inhibitors & Agonists.

Product Name	:	TPX-0131
Cat. No.	:	PC-72509
CAS No.	:	2648641-36-3
Molecular Formula	:	$C_{21}H_{20}F_3N_5O_3$
Molecular Weight	:	447.418
Target	:	Anaplastic Lymphoma Kinase (ALK)
Solubility	:	10 mM in DMSO



Biological Activity

TPX-0131 (Zotizalkib, TPX0131) is a potent, CNS-penetrant, next-generation inhibitor of wild-type **ALK** (IC50=1.4 nM) and 26 ALK resistance mutations (all IC50=<1-7 nM).
TPX-0131 is highly potent against a broad spectrum of ALK drug-resistant mutations. TPX-0131 inhibited C1156Y, E1210K/S1206C, L1198F/C1156Y, L1196M/L1198F, E1210K, L1196M, T1151M, deleted G1202, S1206R, G1202R/L1198F, F1174L, F1245C, R1275Q, and G1202R ALK mutations with IC50 values of <1 nM.
TPX-0131 had IC50 values of 1 to 2 nM for the following ALK mutations: L1198F, L1152R, F1174S, T1151-L1152 insT, V1180L, G1269A, F1174C.
TPX-0131 was less active against ALK mutations including I1171N, L1152P, D1203N, D1203N/E1210K, and G1269S, with IC50 values of 2-7 nM.
TPX-0131 was determined to be a selective ALK inhibitor by evaluating its potency toward a panel of 373 kinases.
TPX-0131 potently inhibits WT EML4-ALK and EML4-ALK harboring a range of point mutations with significantly greater potency against many key resistance mutations, such as solvent front, gatekeeper, and hinge region mutations, relative to previous generations of ALK inhibitors.
TPX-0131 exhibited more than 90% phosphorylation inhibition of EML4-ALK G1202R/L1196M fusion at a mean free plasma concentration of 19.5 nM, demonstrated tumor growth in the EML4-ALK G1202R/L1196M xenograft model.

References

Brion W Murray, et al. ***Mol Cancer Ther.*** 2021 Sep;20(9):1499-1507.

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