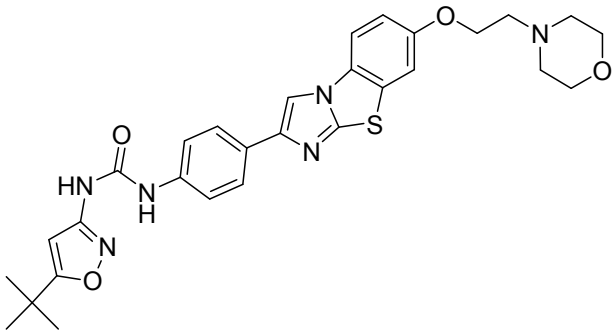
Quizartinib

SYN-1003



1-(5-tert-butylisoxazol-3-yl)-3-[4-[6-(2-morpholinoethoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]phenyl]urea

CAS Registry No.: 950769-58-1

Smiles String:
CC(C)(C)c1cc(no1)NC(=O)Nc2ccc(cc2)c3cn4c5ccc(cc5sc4n3)OCCN6CCOCC6

Molecular Weight: 560.67

Molecular Formula: C29H32N6O4S

Lot Number: Refer to vial

1H-NMR: Available on request

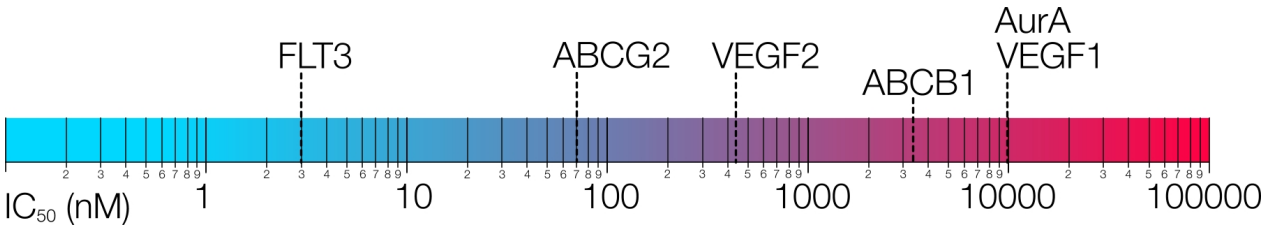
HPLC (Purity): > 95.0% @ 254 nm

ES-MS: Available on request

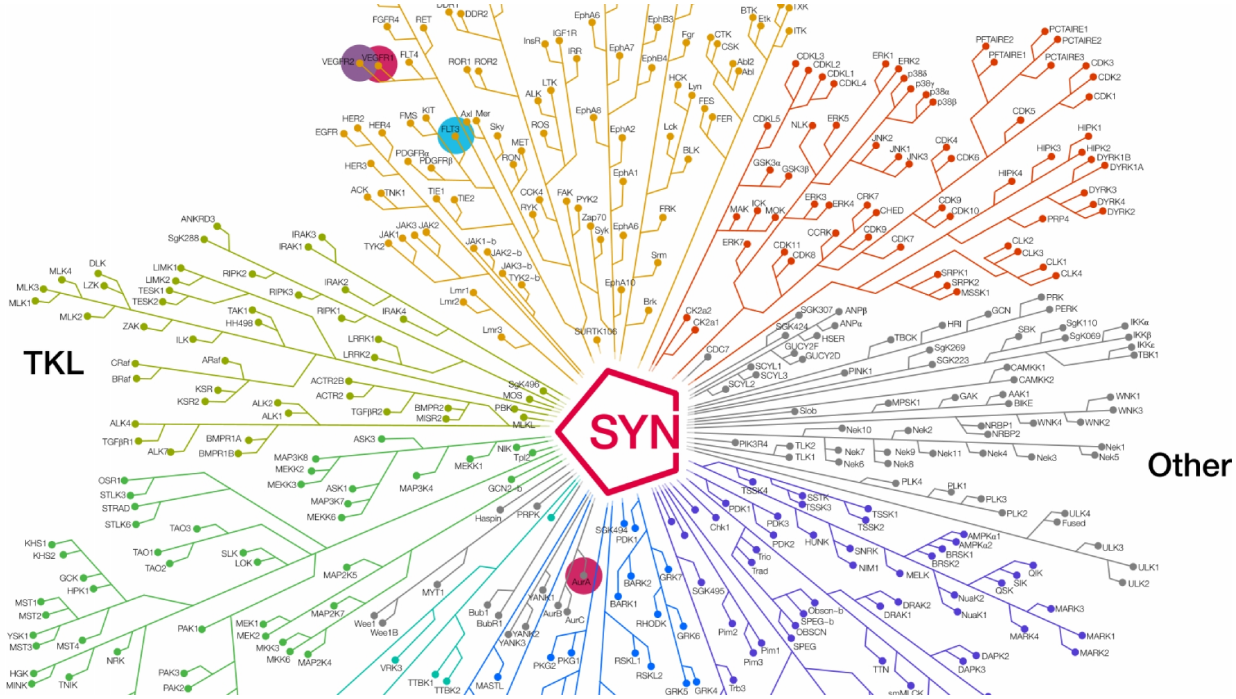
Description:

Quizartinib (AC220) is a second-generation FLT3 inhibitor that has shown promising activity in AML in Phase II clinical trials. It inhibits mutant and wild-type FLT3 in vivo at 0.1 and 0.5 μM, respectively, and has shown favorable activity and tolerability in phase I and II trials in acute myeloid leukemia, with QT prolongation as the dose-limiting toxicity. Recently, AC220 has also been shown to be an effective inhibitor of ATP-binding cassette (ABC) proteins ABCB1 (P-glycoprotein) and ABCG2 (breast cancer resistance protein). Quizartinib inhibited transport of fluorescent ABCG2 and ABCB1 substrates in ABCG2- and ABCB1-overexpressing cells in a concentration-dependent manner, from 0.1 to 5 μM and from 0.5 to 10 μM, respectively, and inhibited [125I]-IAAP photolabeling of ABCG2 and ABCB1 with IC50 values of 0.07 and 3.3 μM, respectively.

Biological Activity



Kinome Mapping



Shipping and Storage Temperature

Shipping:
Ambient

Storage:
2 years -20C, Powder 1 month, -4C in DMSO, More than one month -80C in DMSO

Solubility

DMSO 33 mg/mL, Ethanol 0.5 mg/mL

Preparing Stock Solutions

Stock Solution (1ml DMSO)	1mM	10mM	20mM	50mM
Mass(mg)	0.5606	5.6067	11.2134	28.0335

References

1. Zarrinkar PP, Gunawardane RN, Cramer MD, Gardner MF, Brigham D, Belli B, Karaman MW, Pratz KW, Pallares G, Chao Q, Sprankle KG, Patel HK, Levis M, Armstrong RC, James J, Bhagwat SS . AC220 is a uniquely potent and selective inhibitor of FLT3 for the treatment of acute myeloid leukemia (AML). Blood. 2009 Oct 1;114(14):2984-92. doi: 10.1182/blood-2009-05-222034. Epub 2009 Aug 4.

2. Hsu JT, Yeh TK, Yen SC, Chen CT, Hsieh SY, Hsu T, Lu CT, Chen CH, Chou LH, Chiu CH, Chang YI, Tseng YJ, Yen KR, Chao YS, Lin WH, Jiaang WT . 3-Phenyl-1H-5-pyrazolylamine-based derivatives as potent and efficacious inhibitors of FMS-like tyrosine kinase-3 (FLT3). Bioorg Med Chem Lett. 2012 Jul 15;22(14):4654-9. doi: 10.1016/j.bmcl.2012.05.116. Epub 2012 Jun 7.

Ordering Information

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