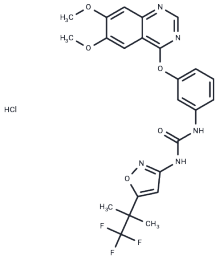
Data Sheet (Cat.No.T14928)

TargetMol

Agerafenib hydrochloride

Chemical Properties



CAS No. : 1227678-26-3

Formula: C24H23ClF3N5O5

Molecular Weight: 553.92

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Agerafenib hydrochloride, a highly potent inhibitor of BRAFV600E (Kd: 14 nM), demonstrates significant efficacy.
Targets(IC50)	Raf,c-RET,c-Kit
In vitro	Agerafenib exhibits high potency against several BRAF V600E-dependent cell lines and selective cytotoxicity for tumor cell lines expressing mutant BRAF V600E. It shows potent binding (BRAF V600E, Kd: 14 nM) and cellular activity (pMEK IC50=82 nM and A375 proliferation IC50=78 nM), with activity in the proliferation assay. Agerafenib also exhibits a favorable CYP450 inhibition profile, with measured IC50 values greater than 10 μM versus the CYP1A2, CYP2C9, CYP2D6, and CYP3A4 isoforms and an IC50=3.4 μM versus CYP2C19.
In vivo	Agerafenib exhibits an exceptional PK profile in mouse, dog, and cynomolgus monkey. Administration of Agerafenib to beagle dogs (single dose of 1 mg/kg i.v and 10 mg/kg p.o) results in low clearance (CL=5.0 (mL/min)/kg) and excellent bioavailability (% F=100). Similarly, in cynomolgus monkey, the administration of Agerafenib (single dose of 1 mg/kg i.v and 10 mg/kg p.o) leads to high oral exposure due to low clearance (CL=6.7 mL/min/kg) and excellent bioavailability (%F=100). Oral administration of Agerafenib to Colo-205 tumor xenograft-bearing mice results in significant inhibition of pMEK in tumor cell lysates.

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8053 mL	9.0266 mL	18.0531 mL
5 mM	0.3611 mL	1.8053 mL	3.6106 mL
10 mM	0.1805 mL	0.9027 mL	1.8053 mL
50 mM	0.0361 mL	0.1805 mL	0.3611 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Rowbottom MW, et al. Identification of 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(1,1,1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea hydrochloride (CEP-32496), a highly potent and orally efficacious inhibitor of V-RAF murine sarcoma viral oncogene homologue B1 (BRAF) V600E.