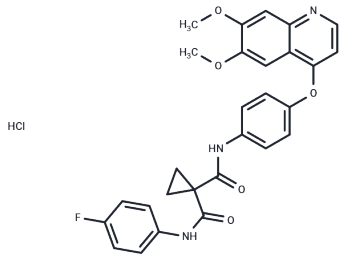
Data Sheet (Cat.No.T5164)

TargetMol
YOUR TARGET MOLECULES

Cabozantinib hydrochloride

Chemical Properties



CAS No. : 1817759-42-4

Formula: C28H25ClFN3O5

Molecular Weight: 537.96

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Cabozantinib hydrochloride (XL184) is a potent pan-tyrosine kinases inhibitor that inhibits VEGFR2, c-Met, Kit, Axl, and Flt4 (IC50s: 0.035, 1.3, 4.6, 7 and 6 nM).
Targets(IC50)	VEGFR,FLT,c-Met/HGFR,TAM Receptor,c-Kit,ROR
In vitro	SR1001 binds specifically to the ligand-binding domains of RORα and RORγt, inducing a conformational change within the ligand-binding domain, resulting in suppression of the receptors' transcriptional activity. SR1001 inhibited the development of murine T(H)17 cells. Furthermore, SR1001 inhibited the expression of cytokines when added to differentiated murine or human T(H)17 cells [1]. Treatment with the RORγT inhibitor SR1001 to abrogate Th17 cell function reduced Th17-dependent learned helplessness [2].
In vivo	After myelin oligodendrocyte glycoprotein (MOG35-55) immunization at day 0, experimental autoimmune encephalomyelitis (EAE) mice were treated with SR1001 (25 mg/kg, b.i.d. i.p.) for the duration of the study. Further analysis of spinal cords from mice harvested at day 18 post-immunization revealed that SR1001 repressed Il17a mRNA expression by ~60%, as well as reduced Il21, and Il22 mRNA expression [1]. When these mice were injected with SR1001, the circadian rhythm of CS expression was eliminated [3].
Cell Research	CD4+ T cells were isolated as described previously and in the Supplementary Materials. CD4+ T cells cultured with splenic feeder cells were activated with 2.5 μg/mL of anti-CD3 (clone 145-11), and differentiated to Th17 cells by addition of IL-6 (20 ng/mL; Peprotech), TGFβ (5 ng/mL), anti-IL-4 (10 μg/mL; clone 11B11, UAB core facility) and anti-IFNγ (10 μg/mL; clone XMG1.2, UAB core facility). After 5 days of differentiation toward Th17 cells, cells were recovered after histopaque gradient purification and resuspended in PBS. An aliquot of cells was used to evaluate the percent of Th17 cells (~40%) and ~10-20×106 undifferentiated CD4+ T or Th17 cells were injected in 500 μL PBS by tail vein 48 h prior to behavioral testing. Where indicated, mice were injected intraperitoneally with 100 μg anti-IL-17A, or 125 μg SR1001 daily beginning 1 day before Th17 cell transfer, and this was continued throughout the experiment. As controls, mice were injected i.v. with ~10-20×106 CD4+ T cells to evaluate the effect of non-differentiated cells, or with 500 μL PBS to mimic the stress of tail vein i.v. injection 48 h prior to behavioral testing. Intracellular cytokine staining was carried out as described previously and in the Supplementary Information [2].

Animal Research	For circadian gene expression experiments male C57BL6 mice (8-10 weeks of age) were either maintained on a L:D (12h：12h) cycle or on constant darkness (1 day). At the circadian time (CT) 0 animals were administered a single dose of 25 mg/kg SR1001 (i.p.) and groups of animals (n?=?6) were sacrificed at CT0, CT6, CT12, and CT18. Gene expression was determined by real-time qPCR. Gene expression was normalized to Cyclophin b in all experiments [3].

Solubility Information

Solubility	DMSO: 5.38 mg/mL (10 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8589 mL	9.2944 mL	18.5887 mL
5 mM	0.3718 mL	1.8589 mL	3.7177 mL
10 mM	0.1859 mL	0.9294 mL	1.8589 mL
50 mM	0.0372 mL	0.1859 mL	0.3718 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.

Reference

Yakes FM, et al. Cabozantinib (XL184), a novel MET and VEGFR2 inhibitor, simultaneously suppresses metastasis, angiogenesis, and tumor growth. Mol Cancer Ther, 2011, 10(12), 2298-2308.