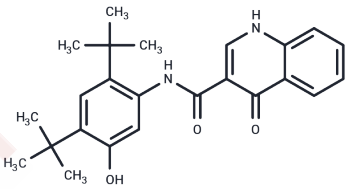
Data Sheet (Cat.No.T2588)

TargetMol

Ivacaftor

Chemical Properties



CAS No. : 873054-44-5

Formula: C24H28N2O3

Molecular Weight: 392.49

Appearance: no data available

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

Biological Description

Description	Ivacaftor (VX-770) (VX-770) is a potentiator of CFTR targeting G551D-CFTR (EC50: 100 nM) and F508del-CFTR (EC50: 25 nM) in Fisher rat thyroid cells, respectively.
Targets(IC50)	CFTR,Autophagy
In vitro	VX-770 increased the forskolin-stimulated IT in temperature-corrected F508del-FRT cells by ~6-fold with an EC50 of 25 ± 5 nM. Before the addition of VX-770, the CFTR channel was exposed to maximally effective concentrations of PKA (75 nM) and ATP (1 mM). Under these conditions, 10 μM VX-770 increased the Po of G551D CFTR by ~6-fold [1]. HEK293 cells transiently expressing ABCB4-wt or the mutants were treated with 10 μmol/L of ivacaftor (VX-770), for 24 hours. Treatment with ivacaftor increased the PC secretion activity by 3-fold for ABCB4-G535D, 13.7-fold for ABCB4-G536R, 6.7-fold for ABCB4-S1076C, 9.4-fold for ABCB4-S1176L and 5.7-fold for ABCB4-G1178S [2].
In vivo	In a rat dose proportionality study, the AUC and Cmax were increased linearly after oral administration of Ivacaftor in a suspension vehicle at doses from 1 to 200 mg/kg (3, 10, 30, and 100 were the intermediate doses). A similar trend was observed in beagle dogs increasing the oral dose from 3 to 80 mg/kg (10, 30, and 60 were the intermediate doses), confirming high levels of oral absorption. The predicted human hepatic clearance of Ivacaftor using allometric scaling from four species was 4.7 mL min?1 kg?1, which is approximately 23% of hepatic blood flow [3].
Cell Research	HEK293 cells were seeded on poly-lysine precoated six-well plates at a density of 1.3 x 10^6 cells/well. Six hours after seeding, cells were transiently transfected with 1μg of ABCB4-encoding plasmids using Turbofect, following the manufacturer's instructions. Twenty-four hours post-transfection, cells were washed twice with HBSS, then the medium was replaced by phenol red-free DMEM containing 0.5 mmol/L sodium taurocholate and 0.02% fatty acid-free bovine serum albumin (BSA) in the presence or absence of 10 μmol/L of ivacaftor, 50 μM/L of UDCA, and 10 μmol/L of ivacaftor plus 50 μM/L of UDCA. Media were collected after 24 hours [2].
Animal Research	Male mouse,Sprague?Dawley rats,beagle dog,and cynomolgus monkeys (n = 3/group) were administered a single iv dose of compound formulated in dimethyl isosorbide/ethanol/PEG400/5% dextrose in water (D5W) (10%/15%/35%/40%) at the nominal dose indicated in a dose volume of 1 mL/kg.Blood samples (0.3 mL,sodium heparin anticoagulant) were collected from an indwelling carotid cannula at the following nominal time points: at predose,5,15,30,and 45 min and 1,2,4,6,8,12,24,36,

and 48 h following iv administration and at predose,0.25,0.50,1,1.5,2,4,8,12,and 24 h following oral administration.The concentration of compound in the plasma samples was determined with a liquid chromatography/tandem mass spectrometry (LC/MS/MS) method,which had a lowest limit of quantitation (LLOQ) of 1 ng/mL and a linearity range between 1 and 2500 ng/mL [3].

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 55 mg/mL (140.13 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5478 mL	12.7392 mL	25.4784 mL
5 mM	0.5096 mL	2.5478 mL	5.0957 mL
10 mM	0.2548 mL	1.2739 mL	2.5478 mL
50 mM	0.051 mL	0.2548 mL	0.5096 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

Van Goor F, et al. Rescue of CF airway epithelial cell function in vitro by a CFTR potentiator, VX-770. Proc Natl Acad Sci U S A. 2009 Nov 3;106(44):18825-30.

Sondo E, Cresta F, Pastorino C, et al. The L467F-F508del Complex Allele Hampers Pharmacological Rescue of Mutant CFTR by Elexacaftor/Tezacaftor/Ivacaftor in Cystic Fibrosis Patients: The Value of the Ex Vivo Nasal Epithelial Model to Address Non-Responders to CFTR-Modulating Drugs. International Journal of Molecular Sciences. 2022, 23(6): 3175.

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Non-canonical hepatic androgen receptor mediates glucagon sensitivity in female mice through the PGC1α/ERRα/mitochondria axis