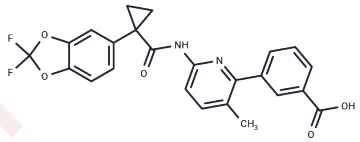
Data Sheet (Cat.No.T2595)

TargetMol

Lumacaftor

Chemical Properties



CAS No. : 936727-05-8

Formula: C24H18F2N2O5

Molecular Weight: 452.41

Appearance: no data available

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

Biological Description

Description	Lumacaftor (VRT 826809) is a CFTR modulator that corrects the folding and trafficking of CFTR protein. It enhances F508del-CFTR protein maturation in FRT cells (EC50: 100 nM).
Targets(IC50)	CFTR,Autophagy
In vitro	In cultured human bronchial epithelial cells isolated from patients with CF homozygous for F508del, Lumacaftor (VX-809) improved F508del-CFTR processing in the endoplasmic reticulum and enhanced chloride secretion to approximately 14% of non-CF human bronchial epithelial cells (EC50: 81 nM), a level associated with mild CF in patients with less disruptive CFTR mutations [1]. VX-809 produced a concentration-dependent increase in the HRP luminescence signal after incubation with cells at 37°C or 27°C in both cell lines, with a similar EC50 value of approximately 0.3 μM [2].
Kinase Assay	In one set of assays, R1070W-?F508-CFTR-HRP (R1070W-HRP)-expressing CFBE41o? cells were incubated with 100 μl medium containing 25 μM test compounds and 0.5 μg/ml doxycycline for 24 hours at 37°C. In a second set of assays, ?F508-CFTR-HRP (?F508-HRP) -expressing CFBE41o? cells were incubated with 100 μl medium containing 25 μM test compounds, 2 μM VX-809, and 0.5 μg/ml doxycycline for 24 hours at 37°C. All compound plates contained negative controls (DMSO vehicle) and positive controls [2 μM VX-809]. In both assays, the cells were washed four times with PBS, and HRP activity was assayed by the addition of 50 μl/well of HRP substrate. After shaking for 5 minutes, chemiluminescence was measured using a Tecan Infinite M1000 plate reader (Tecan Groups Ltd, Mannedorf, Switzerland) equipped with an automated stacker (integration time, 100 milliseconds). Z′ is defined as = 1 ? [(3 × standard deviation of maximum signal control + 3 × standard deviation of minimum signal control)/absolute (mean of maximum signal control ? mean of minimum signal control)] [2].
Cell Research	FRT, HEK-293, or HBE cells expressing CFTR or F508del-CFTR were incubated for 24 h at 37 °C with or without VX-809 in the assay media. After incubation, cells were harvested in ice-cold D-PBS solution (without calcium and magnesium) and pelleted at 1,000 × g at 4 °C. Cell pellets were lysed in 1% Nonidet P-40, 0.5% sodium deoxycholate, 200 mM NaCl, 10 mM Tris, pH 7.8, and 1 mM EDTA plus protease inhibitor mixture (1:250) for 30 min on ice. Lysates were spun for 10 min at 10,000 × g at 4 °C to pellet nuclei and insoluble material. Approximately 12 μg total protein was heated in Laemmli buffer with 5% β-mercaptoethanol at 37 °C for 5 min and loaded onto a 3% to 8% Tris-acetate gel. The gel was transferred to nitrocellulose and processed for Western blotting by using monoclonal CFTR antibody 769 or polyclonal to GAPDH. Blots were developed by

enhanced chemiluminescence. Quantification of the relative amounts of bands C and GAPDH was performed by using NIH ImageJ analysis of scanned films [1].

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 6 mg/mL (13.26 mM),Sonication is recommended. DMSO: 50 mg/mL (110.52 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2104 mL	11.0519 mL	22.1038 mL
5 mM	0.4421 mL	2.2104 mL	4.4208 mL
10 mM	0.221 mL	1.1052 mL	2.2104 mL
50 mM	0.0442 mL	0.221 mL	0.4421 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. Correction of the F508del-CFTR protein processing defect in vitro by the investigational drug VX-809. Proc Natl Acad Sci U S A. 2011 Nov 15;108(46):18843-8.
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.
Baldassarri M, Zguro K, Tomati V, et al.Gain-and Loss-of-Function CFTR Alleles Are Associated with COVID-19 Clinical Outcomes.Cells.2022, 11(24): 4096.
Phuan PW, et al. Synergy-based small-molecule screen using a human lung epithelial cell line yields ΔF508-CFTR correctors that augment VX-809 maximal efficacy. Mol Pharmacol. 2014 Jul;86(1):42-51.
Tomati V, Costa S, Capurro V, et al.Rescue by elexacaftor-tezacaftor-ivacaftor of the G1244E cystic fibrosis mutation's stability and gating defects are dependent on cell background.Journal of Cystic Fibrosis.2022