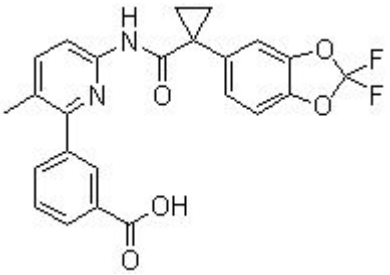
Product Introduction

VX-809 (Lumacaftor)

VX-809 acts to correct **CFTR** mutations common in cystic fibrosis by increasing mutant CFTR (F508del-CFTR) maturation,**EC50** of 0.1 μM. Phase 3.

Technical Data:

Molecular Weight (MW):	452.41	
Formula:	$C_{24}H_{18}F_2N_2O_5$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 90 mg/mL	
	Water <1 mg/mL	
	Ethanol 6 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	936727-05-8	

Biological Activity

VX-809 acts at the level of the ER to allow a fraction of the F508del-CFTR to adopt a properly folded form, to exit the ER and mobilize to the cell surface for normal functioning. In Fischer rat thyroid (FRT) cells expressing F508del-CFTR, VX-809 treatment significantly improves F508del-CFTR maturation by 7.1 fold with an EC50 of 0.1 μM, and enhances F508del-CFTR-mediated chloride transport by approximately 5 fold with EC50 of 0.5 μM, while VRT-768 has higher EC50 values of 7.9 μM and 16 μM, respectively. In HEK-293 cells expressing F508del-CFTR, VX-809 (3 μM) treatment increases F508del-CFTR exit from the ER by 6

fold, reaching levels comparable to 34% of CFTR. In primary human bronchial epithelial (HBE) cells with F508del-CFTR mutation, VX-809 increases CFTR maturation and enhances chloride secretion with EC50 of 350 nM and 81 nM, respectively, more efficacious than Corr-4a and VRT-325. F508del-CFTR corrected by VX-809 exhibits single-channel open probability of 0.39 similar to normal CFTR of 0.40. Unlike VX-770, VX-809 is not a CFTR potentiator, as acute addition of VX-809 has no effect on F508del-CFTR function. In contrast to VRT-325 and Corr-4a, VX-809 does not improve the processing of the normal or mutant forms of hERG or P-gp, as well as other disease-causing mislocalized proteins, including α1-antitrypsin Z mutant (E342K-α1-AT) or N370S-β-glucosidase, suggesting that VX-809 is specific for CFTR. VX-809 in combination with VRT-325 or Corr-4a has additive effect on CFTR-mediated chloride transport in cultured F508del-HBE. [1]

Higher specificity and efficacy relative to other CFTR defect drugs.

References

[1] Van Goor F, et al. Proc Natl Acad Sci U S A, 2011, 108(46), 18843-18848.

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