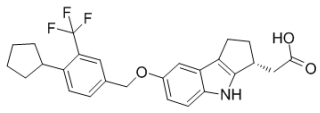
Data Sheet

Product Name:	Etrasimod
Cat. No.:	HY-12789
CAS No.:	1206123-37-6
Molecular Formula:	$C_{26}H_{26}F_3NO_3$
Molecular Weight:	457.48
Target:	LPL Receptor
Pathway:	GPCR/G Protein
Solubility:	DMSO: ≥ 28 mg/mL



BIOLOGICAL ACTIVITY:

Etrasimod (APD334) is a potent, selective and orally available antagonist of the sphingosine–1–phosphate–1 (**$S1P_1$**) receptor with an **IC_{50}** value of 1.88 nM in CHO cells.

IC50 & Target: IC50: 1.88 nM (S1P1)[1]

In Vitro: APD334 is a structurally novel, selective, functional antagonist of $S1P_1$. In CHO cells expressing HA tagged $S1P_1$, APD334 is found to have an IC_{50} value of 1.88 nM. Moderate agonism at human $S1P_4$ and $S1P_5$ is observed but is reduced relative to $S1P_1$, both in terms of potency and efficacy. APD334 is devoid of any agonism or antagonism at human $S1P_2$ and $S1P_3$. APD334 achieves good central exposure following oral dosing and possesses a favorable pharmacokinetic profile in multiple preclinical species. $S1P_1$ activity is maintained in mice (EC_{50}=0.44 nM), rats (EC_{50}=0.32 nM), dogs (EC_{50}=0.34 nM) and monkeys (EC_{50}=0.32 nM)[1].

In Vivo: APD334 has a relatively low systemic clearance (<4% of hepatic blood flow) and high C_{max} across all species. In both dog and monkey a significant decrease in volume of distribution (Vss) is observed relative to rodent. Oral bioavailability is in the range of 40–100%, and the terminal phase half–life varied from 6 h in monkey, to as long as 29 h in dog. Rat and monkey $t_{1/2}$ values for siponimod (another S1P1 modulator currently in human trials) have been disclosed and are 6 and 19 h, respectively[1].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: [1]Rat: APD334 induced effects on blood lymphopenia are determined in male Sprague–Dawley rats. Briefly, male rats are given a 0 (vehicle only), 0.03 (mice only), 0.1, 0.3 or 1 mg/kg oral dose of APD334 formulated in 0.5% methylcellulose (MC) in water. Rat blood samples are collected at 0, 1, 3, 5, 8, 16, 24, 32, 48 and 72 hours post–dose[1].

Mouse: APD334 induced effects on blood lymphopenia are determined in male BALB/c mice. Briefly, male mice are given a 0 (vehicle only), 0.03 (mice only), 0.1, 0.3 or 1 mg/kg oral dose of APD334 formulated in 0.5% methylcellulose (MC) in water. Mouse blood samples are taken at 0, 1, 3, 5, 8, 16, 24 and 32 hours post–dose[1].

References:

[1]. Buzard DJ, et al. Discovery of APD334: Design of a Clinical Stage Functional Antagonist of the Sphingosine–1–phosphate–1 Receptor. ACS Med Chem Lett. 2014 Nov 4;5(12):1313–7.

Caution: Product has not been fully validated for medical applications. For research use only.

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