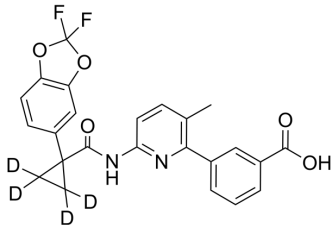
Lumacaftor-d_4

Cat. No.:	HY-13262S
CAS No.:	2733561-44-7
Molecular Formula:	$C_{24}H_{14}D_4F_2N_2O_5$
Molecular Weight:	456.43
Target:	Isotope-Labeled Compounds
Pathway:	Others
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (219.09 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1909 mL	10.9546 mL	21.9092 mL
	5 mM	0.4382 mL	2.1909 mL	4.3818 mL
	10 mM	0.2191 mL	1.0955 mL	2.1909 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Lumacaftor-d_4 is the deuterium labeled Lumacaftor (HY-13262)[1].

In Vitro

Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug molecules, largely as tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to affect the pharmacokinetic and metabolic profiles of drugs[1].

In fischer rat thyroid (FRT) cells, Lumacaftor improves F508del-CFTR maturation by 7.1±0.3 fold (n=3) compared with vehicle-treated cells (EC_{50}, 0.1±0.1 μM; n=3) and enhances F508del-CFTR-mediated chloride transport by approximately fivefold (EC_{50}, 0.5±0.1 μM; n=3). At Lumacaftor concentrations greater than 10 μM, the response is reduced, resulting in a bell-shaped dose-response relationship with an IC_{50} of approximately 100 μM. Lumacaftor is orally bioavailable in rats and achieved in vivo plasma levels significantly above concentrations required for in vitro efficacy[2]. Lumacaftor produces 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 EC_{50} value of approximately 0.3 μM. In F508-HRP CFBE41o$^-$ cells at 37°C, Lumacaftor increases the signal maximally to approximately 250 luminescence arbitrary units (a.u.) over the DMSO control baseline of approximately 60 a.u., representing an approximately 4-fold signal increase. Similarly, with the R1070W-HRP CFBE41o$^-$ cells, Lumacaftor increases the signal maximally to approximately 220 a.u. over the DMSO control baseline of approximately 85 a.u., representing an

	approximately 2.5-fold signal increase. Therefore, both cell lines produced robust signals with a good dynamic range for high-throughput screening[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Oral dosing of 1 mg/kg Lumacaftor in male Sprague-Dawley rats results in a C_{max} of 2.4±1.3 μM with a $t_{1/2}$ of 7.7±0.4 h (mean±SD; n=3), indicating that that Lumacaftor is orally bioavailable and able to reach plasma levels that significantly exceeded EC_{50}s for F508del-CFTR correction[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Russak EM, et al. Impact of Deuterium Substitution on the Pharmacokinetics of Pharmaceuticals. Ann Pharmacother. 2019 Feb;53(2):211-232.

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