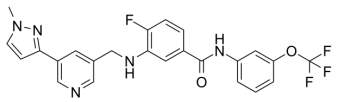
VU6015929

Cat. No.:	HY-135401
CAS No.:	2442597-56-8
Molecular Formula:	$C_{24}H_{19}F_4N_5O_2$
Molecular Weight:	485.43
Target:	Discoidin Domain Receptor
Pathway:	Protein Tyrosine Kinase/RTK
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 : 250 mg/mL (515.01 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0600 mL	10.3001 mL	20.6003 mL
	5 mM	0.4120 mL	2.0600 mL	4.1201 mL
	10 mM	0.2060 mL	1.0300 mL	2.0600 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.28 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.28 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

VU6015929 is a potent, selective and orally active dual discoidin domain receptor 1/2 (DDR1/2) inhibitor with IC_{50}s of 4.67 nM and 7.39 nM, respectively. VU6015929 potently blocks collagen-induced DDR1 activation and collagen-IV production[1].

IC_{50} & Target

DDR1	DDR2
4.67 nM (IC_{50})	7.39 nM (IC_{50})

In Vitro

VU6015929 (Compound 7e; 4-100 nM; 24 hours; HEK293-DDR1b cells) treatment inhibits collagen I-induced DDR1 phosphorylation in a dose dependent manner. Analysis of the phosphorylated DDR1/total DDR1 ratio reveals an IC_{50} for VU6015929 of 0.7078 nM[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	HEK293-DDR1b cells
Concentration:	4 nM, 20 nM, 100 nM
Incubation Time:	24 hours
Result:	Inhibited collagen I-induced DDR1 phosphorylation in a dose dependent manner. Significantly inhibited collagen IV production.

In Vivo

VU6015929 (Compound 7e) is further evaluated in a rat IV (0.5 mg/kg)/PO (3 mg/kg) PK study in a 10% EtOH/40% PEG400/50% saline vehicle. VU6015929 displays a good in vitro:in vivo correlation (IVIC), with moderate in vivo clearance (CL_p = 34.2 mL/min/kg), an ~3 hour half-life, moderate volume of distribution at steady state (V_{ss} = 4.3 L/kg) and 12.5% oral bioavailability with a rapid T_{max} (0.75 hr)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Daniel E. Jeffries, et al. Discovery of VU6015929: A Selective Discoidin Domain Receptor 1/2 (DDR1/2) Inhibitor to Explore the Role of DDR1 in Antifibrotic Therapy. ACS Med. Chem. Lett. 2019.

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