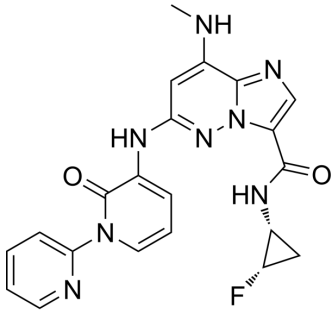
Tyk2-IN-5

Cat. No.:	HY-111745
CAS No.:	1797432-62-2
Molecular Formula:	$C_{21}H_{19}FN_8O_2$
Molecular Weight:	434.43
Target:	JAK
Pathway:	Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 43.33 mg/mL (99.74 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3019 mL	11.5093 mL	23.0187 mL
	5 mM	0.4604 mL	2.3019 mL	4.6037 mL
	10 mM	0.2302 mL	1.1509 mL	2.3019 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: ≥ 2.17 mg/mL (5.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tyk2-IN-5 (compound 6) is a potent, selective and orally active tyrosine kinase 2 (Tyk2) inhibitor that acts on the JH2 structural domain. Tyk2-IN-5 shows a K_i value of 0.086 nM for Tyk2 JH2 and an IC_{50} value of 25 nM for IFNα. Tyk2-IN-5 efficiently inhibits the production of IFNγ in a pharmacodynamic rat model and is fully efficacious in a rat model of arthritis [1].

IC_{50} & Target

Tyk2 JH2	IFNα
0.086 nM (Ki)	25 nM (IC_{50})

In Vitro

Tyk2-IN-5 inhibits Jak1-3 with IC_{50} values of >2 μM and displays the Jak1-3 dependent cellular activities of >12.5 μM (IC_{50} values)[1].

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

In Vivo

Tyk2-IN-5 (5, 10 mg/kg; p.o.; twice daily for 20 days) shows highly efficacious in a rat adjuvant arthritis model[1].
Tyk2-IN-5 (1, 10 mg/kg; p.o.; single) inhibits IL-12/IL-18 induced IFNγ production in a dose-dependent manner[1].
Tyk2-IN-5 (10 mg/kg; p.o.; single) shows a high oral exposure and bioavailability (114%) in rat[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Lewis male rats (rat adjuvant arthritis model)[1].
Dosage:	5, 10 mg/kg
Administration:	Oral administration; twice daily for 20 days
Result:	Demonstrated full efficacy to prevent the rats' paw from swelling.

Animal Model:	Lewis male rats (IL-12/IL-18-induced)[1].
Dosage:	1, 10 mg/kg
Administration:	Oral administration; single
Result:	Inhibited IL-12/IL-18 induced IFNγ production by 45% and 77% at doses of 1 and 10 mg/kg, respectively.

Animal Model:	Lewis male rats, mouse[1].
Dosage:	10 mg/kg
Administration:	Oral administration; single
Result:	Pharmacokinetic Parameters of Tyk2-IN-5 in mouse and rat[1].

	PO (10 mg/kg)	
	mouse	rat
C_{max} (μM)	15	9.4
AUC_{0-24} (μM•h)	19	57
CL (mL/min/kg)	16	7.8
F (%)	86	114

REFERENCES

[1]. Liu C, et al. Identification of Imidazo[1,2-b]pyridazine Derivatives as Potent, Selective, and Orally Active Tyk2 JH2 Inhibitors. ACS Med Chem Lett. 2019 Feb 21;10(3):383-388.

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

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