HPK1-IN-7

Cat. No.: HY-138742

CAS No.: 2320462-65-3

Molecular Formula: $C_{24}H_{22}N_6O_4$

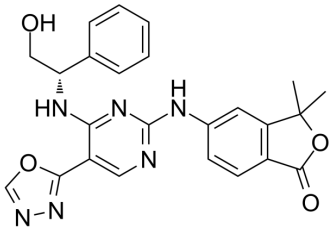
Molecular Weight: 458.47

Target: MAP4K

Pathway: MAPK/ERK Pathway

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 : 125 mg/mL (272.65 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1812 mL	10.9058 mL	21.8117 mL
5 mM	0.4362 mL	2.1812 mL	4.3623 mL
10 mM	0.2181 mL	1.0906 mL	2.1812 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 (4.54 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

HPK1-IN-7 is a potent, orally active HPK1 (hematopoietic progenitor kinase 1, MAP4K1) inhibitor (IC_{50}=2.6 nM) with excellent family and kinome selectivity. HPK1-IN-7 shows selectivity against IRAK4 (59 nM) and GLK (140 nM). HPK1-IN-7 shows robust efficacy against MC38 syngeneic tumor model in combination with anti-PD1[1].

IC_{50} & Target

HPK1 2.6 nM (IC_{50})	GLK/MAP4K3 140 nM (IC_{50})	IRAK4 59 nM (IC_{50})	Fms/CSFR 3.2 nM (IC_{50})
FLT3 25.4 nM (IC_{50})	AMPKA1 44.3 nM (IC_{50})	cKIT 45.7 nM (IC_{50})	MST1 55.1 nM (IC_{50})
ICK 65.1 nM (IC_{50})	MST2 78.5 nM (IC_{50})		

In Vivo

HPK1-IN-7 (100 mg/kg; p.o.; twice daily for 28 days) shows robust enhancement of anti-PD1 efficacy in a syngeneic tumor model of colorectal cancer[1].

HPK1-IN-7 (compound 24) (1 mg/kg; intravenous; mice) is characterized by moderate plasma clearance (43 mL/min/kg) and a large volume of distribution (4.4 L/kg). After oral administration (20 mg/kg), the Cmax was 5.3 μM and the $AUC_{0\text{-}24h}$ was 19 μM•h. The calculated oral bioavailability based on these pharmacokinetics studies is approximately 100%[1].

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

Animal Model:	Mice (MC38 syngeneic tumor model)[1]
Dosage:	100 mg/kg
Administration:	Oral; twice daily for 28 days
Result:	Enhanced the efficacy of anti-PD1 treatment, garnering a 100% cure rate vs a 20% cure rate with anti-PD1 alone.

REFERENCES

[1]. Degnan AP, et al. Discovery of Orally Active Isofuranones as Potent, Selective Inhibitors of Hematopoetic Progenitor Kinase 1. ACS Med Chem Lett. 2021;12(3):443-450. Published 2021 Feb 19.

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